No. 2015-1696

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CORDIS CORPORATION,

Appellant,

v.

BOSTON SCIENTIFIC SCIMED,

Appellee,

ABBOTT LABORATORIES,

Appellee.

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Inter Partes Reexamination Nos. 95/000,542 and 95/000,552

OPENING BRIEF OF APPELLANT CORDIS CORPORATION

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August 17, 2015

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

Cordis Corporation v. Boston Scientific Scimed

No. 2015-1696

CERTIFICATE OF INTEREST

Counsel for the (~~petitioner~~) (appellant) (~~respondent~~) (~~appellee~~) (~~amicus~~) (~~name of party~~) Cordis Corporation certifies the following (use "None" if applicable; use extra sheets if necessary):

1. The full name of every party or amicus represented by me is:

Cordis Corporation

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

Johnson & Johnson

4. ☑ The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

BAKER HOSTETLER LLP: Joseph Lucci, Maurice Valla, John F. Murphy, and Charlie C. Lyu

June 17, 2015
Date

/s/ Joseph Lucci
Signature of counsel

/s/ Joseph Lucci
Printed name of counsel

Please Note: All questions must be answered

cc: All counsel of record via ECF

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STATEMENT OF RELATED CASES

No other appeal in or from this proceeding has previously been before this or any other appellate court. In this appeal, Cordis challenges, *inter alia*, several petition decisions by the Director of the Patent Office denying certain subpoenas. Cordis also challenged the propriety of those denials in *Cordis Corp. v. Lee*, No. 12-cv-75 (E.D. Va.), the final decision in which is now on appeal to this Court in appeal no. 2015-1371 (and cross-appeal no. 2015-1445).

Inter partes reexamination no. 95/000,567, concerning Cordis's United States patent no. 6,746,773 is still pending before the Board, and concerns certain issues similar to those presented in this appeal. Also, the district court litigation styled *Wyeth et al. v. Abbott Labs., et al.*, No. 09-4850 (D.N.J.) involves the patent underlying this appeal, and is stayed pending the reexamination and thus, in turn, will also be affected by the decision in this appeal.

Counsel knows of no other cases pending in this or any other court that will directly affect or be directly affected by this Court's decision in the pending appeal.

JURISDICTIONAL STATEMENT

Pursuant to 28 U.S.C. § 1295(a)(4)(A) and 35 U.S.C. § 141, this Court has jurisdiction over this appeal from a final decision of the Board in a patent reexamination proceeding. The Board had subject matter jurisdiction pursuant to 35 U.S.C. §§ 134, 306, and 315 (2006) over Cordis's appeal from a final rejection in the reexamination proceeding. The Board rendered its final decision on February 27, 2015, and Cordis timely filed this appeal on April 24, 2015. In related appeal no. 2015-1371, Cordis contends that this Court would lack jurisdiction to review the petition decisions in the instant appeal. However, because the Patent Office successfully argued to the district court in *Cordis v. Lee* that this Court would have jurisdiction to review the petition decisions in the instant appeal, Cordis appealed the decisions as a precaution in the instant appeal.

INTRODUCTION

The inventors of Cordis's 844 Patent[1] discovered that a particular copolymer, a VDF:HFP copolymer in an 85:15 ratio, would be remarkably effective for use in drug eluting coronary stents. No one had ever used this copolymer, much less this particular blend, as a sustained release coating in a medical device. Cordis's invention was so compelling that when Abbott developed the drug eluting stent later to be sold by both Abbott and Boston Scientific, it decided to utilize the exact VDF:HFP copolymer in the exact 85:15 ratio taught by the 844 Patent, and then unabashedly touted its use as critical to the product's success.

Not surprisingly, Cordis then sued Abbott and Boston Scientific for infringing the 844 Patent, after which Abbott and Boston Scientific provoked the *inter partes* reexaminations underlying this appeal, while obtaining a stay of the infringement litigation.

The relevant claims of the 844 Patent were finally rejected by the examiner in the *inter partes* reexaminations, and those rejections were later affirmed by the Board. In doing so, the Board based its decision on a combination of three references: the first disclosed a drug-eluting stent and a very long list of possible

[1] United States Patent No. 7,591,844 (JA216-255).

polymers, none of which was the claimed type of copolymer; the second disclosed the claimed type of copolymer among yet another long list of possible choices, but not with the claimed 85:15 monomer blend, in the context of different kinds of medical devices, but not stents; and the third disclosed the claimed 85:15 blend, but in a 50-year old patent for industrial — not medical — applications. Using Cordis's claim as the blueprint, the Board plucked the necessary components from each prior art reference, and pronounced the combination obvious. The Board's analysis was improper and should be reversed.

In connection with the reexaminations, Cordis presented the non-confidential objective evidence of nonobviousness available to it: that Abbott copied the 844 Patent's invention after hiring away one of the inventor's co-workers; that Abbott had given tribute to the invention in its advertising and public statement; and that the Abbott and Boston Scientific stents that embody the patented invention have enjoyed tremendous commercial success. Cordis further sought production of — or permission for its litigation counsel to disclose — internal Abbott and Boston Scientific documents in their possession, including those that may have been produced under the protective order in the infringement litigation. Abbott and Boston Scientific steadfastly (and thus far successfully) resisted these efforts, unapologetically criticizing Cordis's positions as being insufficiently supported due to the lack of internal Abbott or Boston Scientific

documents to confirm Cordis's contentions. In the meantime, the Patent Office erroneously denied Cordis's petitions seeking to subpoena Abbott and Boston Scientific for this vital objective evidence of nonobviousness within their possession.

Abbott and Boston Scientific admit that their stents use the same polymer blend claimed in the 844 Patent. But by taking their invalidity defense out of district court and into *inter partes* reexaminations, Abbott and Boston Scientific have been able to conceal evidence of their copying, unexpected results, and commercial success from the Patent Office.

Recognizing that the nonobviousness of the 844 Patent's inventions cannot be fully and fairly judged in the absence of knowledge of the real world experiences that led to Abbott's infringement, Cordis pursued a number of procedural avenues in the district court and in the Patent Office to ensure that relevant evidence from the litigation will be available to the Patent Office (and to this Court) in determining the obviousness issue. Over the years, Cordis explained to the Patent Office why it needs access to subpoenas in these reexaminations. In response, the Patent Office steadfastly refused to consider Cordis's individual circumstances and issued blanket denials. The Patent Office's denials, and its failure provide a decision on the merits, are arbitrary and capricious. The evidence

is vital, and Cordis should be afforded the subpoenas to introduce the evidence into the record of the pending *inter partes* reexaminations.

Abbott, too, has fought Cordis every step of the way in its attempts to obtain objective evidence of nonobviousness for the record of the *inter partes* reexaminations. But Abbott has never argued that it would be burdensome to produce the objective evidence, nor has Abbott argued that it does not have the evidence. Rather, Abbott has contended that the evidence is confidential, and that entering it into the Patent Office record would reveal it to the public. Abbott's confidentiality concerns, however, are baseless, because the Patent Office already has mechanisms in place for handling confidential information.

Because of the Patent Office's arbitrary and capricious refusal to allow Cordis access to subpoenas in the underlying reexaminations, Abbott and Boston Scientific kept their experts in ignorance of the objective evidence, so they were free to testify without having to take such evidence into account, meaning that the examiner and Board were presented with an incomplete record. The Board's decision shows the impact of this record, because the Patent Office repeatedly found deficiencies in Cordis's arguments based on the objective evidence, observing, for example, that Cordis lacked evidence of Abbott and Boston Scientific's copying.

The Board's decision should be reversed because the prior art would not

have led a person of ordinary skill in the art to the claimed invention. At a minimum, the Board's decision should be vacated and remanded so that Cordis can supplement the obviousness record with the objective evidence in Abbott's and Boston Scientific's possession, and the Patent Office can judge Cordis's claims on a fair and complete record.

STATEMENT OF THE ISSUES

In the Merged Reexaminations of Cordis's 844 Patent:

(1) did the Board erroneously rely on hindsight in affirming the examiner's rejection of claims 1-17 and 19-23 as obvious; and

(2) were the Patent Office's denials of Cordis's petitions for subpoenas to obtain vital evidence of nonobviousness from the third-party requesters arbitrary and capricious under the APA?

STATEMENT OF THE CASE

A. Cordis's Pioneering Work Led to the Patented Drug-Eluting Polymer-Coated Stents Underlying this Appeal

Percutaneous transluminal coronary angioplasty ("PTCA") is a well-accepted, non-surgical technique for treating the narrowing and constriction of coronary arteries associated with atherosclerotic coronary artery disease. JA3718 & JA3732 at ¶ 21. During PTCA, a catheter with a small balloon on its tip is inserted into the narrowed ("stenosed") artery. JA3732 at ¶ 21. The balloon is then inflated under high pressure to fracture or compress the atherosclerotic plaque, thereby widening the artery and increasing blood flow to the heart. *Id.* Subsequently, one or more "stents" — tiny, spring-like tubes made from metal or alloys — are placed in the artery to keep the artery open, improve blood flow, and prevent the artery from collapsing. *Id.* First approved by the FDA in 1994, "bare-metal" coronary stents were pioneered and developed by Johnson & Johnson together with Julio Palmaz, M.D. *Id.*

Restenosis ("re-narrowing") is a complication associated with PTCA that occurs in approximately 20-30% of patients who receive an intravascular stent. JA3732 at ¶ 22. Restenosis results in new blockages of the coronary artery at the angioplasty site. *Id.* In-stent restenosis is caused primarily by intimal hyperplasia, the growth of smooth muscle cells, fibroblasts and extracellular matrix into the

lumen of the blood vessel caused by the wound-healing process associated with PTCA-mediated vascular injury. *Id.*

To solve the problem of restenosis, Cordis (an owner of the 844 Patent) developed the Cypher® coronary stent. JA3732 at ¶ 23. Approved in April 2003, the Cypher® stent was the first drug-eluting stent to be approved by the FDA and sold in the United States. *Id.* In the Cypher® stent, a version of the drug rapamycin, sirolimus, is combined with a polymer blend of two non-erodible polymers (*i.e.*, polyethylene-co-vinyl acetate and poly n-butyl methacrylate) to form the basecoat which is applied to the stent. JA3732 at ¶ 24.

Concomitant with the development of the Cypher® stent, Cordis also worked with Johnson & Johnson's Corporate Biomaterials Center to develop alternate polymer coatings for use in drug-eluting stents. JA3732 at ¶ 26. This resulted in Cordis's discovery of the use of a copolymer comprising vinylidinefluoride ("VDF") and hexafluoropropylene ("HFP") with a weight percent ratio of VDF:HFP of about 85:15 as a stent coating, as claimed in the 844 Patent. *Id.*

Selection of a suitable polymer for use as the coating/drug carrier layer requires a careful balancing of properties. JA10277 & JA10254 at ¶ 4. The polymer, for example, must adhere sufficiently well to withstand not only placement and expansion of the stent, but also the shear stresses resulting from

blood flow that are typically found in small coronary arteries. JA10254 at ¶ 5. The polymer must also be one that will not cause adverse reactions when placed in prolonged contact with the endothelial cells that line the internal vessel wall; the polymer additionally must not be thrombogenic under the particular conditions to which the device is exposed. *Id.* And the polymer also must be able to carry and retain a sufficient amount of the drug and release it at an appropriate rate for an extended period of time. JA10254 at ¶ 6.

In the decade preceding the filing date of the 844 Patent, several different companies were working on DES technology, and a number of approaches had been proposed for the design of each of the various stent components. JA10277; *see also* JA8018-8019, JA8051-8054, & JA9715 at ¶ 143. Importantly, not a single prior art reference mentioned using any VDF:HFP copolymer as a sustained release coating for any medical device. JA10277. The inventors discovered that a particular commercially available VDF:HFP copolymer that had never previously been used as a sustained-release drug delivery matrix can be intermixed with a therapeutic agent and applied to a balloon-expandable stent to produce not only an effective stent coating but one that would lead to a commercially successful DES. JA8019 & JA10277.

As an added benefit, the claimed copolymer is able to form an effective stent coating without being heated to a temperature of greater than 60° C during the

coating process or afterward. JA10277-78. This property greatly facilitates the preparation of stents that employ a temperature-sensitive pharmaceutical agent (such as the sirolimus version of rapamycin employed on the Cypher® stent, or the slightly different everolimus analogue of rapamycin used on the stents marketed by Abbott and Boston Scientific). *Id*. Cordis's invention is claimed, *inter alia*, in representative claim 1 of the 844 Patent:

> 1. A device for intraluminal implantation in a vessel comprising a balloon-expandable stent and a pharmaceutical agent-containing coating, said coating comprising a biocompatible polyfluoro copolymer that comprises about eighty-five weight percent vinylidinefluoride [VDF] copolymerized with about fifteen weight percent hexafluoropropylene [HFP] and at least one pharmaceutical agent intermixed with said copolymer, wherein said coating has not been subjected to a maximum temperature greater than 60° C during the coating process or afterward, thereby providing an adherent coating that remains adhered to the device upon expansion of the balloon-expandable stent.

JA254 at col. 37, l. 59- col. 38, l. 3.

Although Abbott and Boston Scientific could have used one of the other polymers disclosed in the prior art, they did not. For their Xience V and Promus DESs, they instead elected to use a copolymer comprising VDF and HFP with a weight percent ratio of VDF:HFP of about 85:15 as a coating for these DESs, exactly the same type of copolymer claimed in the 844 Patent. JA14793 at ll. 4-8, JA10278, JA8031, JA8128 at ll. 13-21 & JA8789-861. Indeed, Abbott even vigorously pursued a patent application containing claims that cover the use as a

stent coating of a VDF:HFP copolymer having particular physical properties — properties that are held by the 85:15 VDF:HFP recited in the 844 Patent claims JA8032-34, JA8770-777 & JA8778-8788.

The Xience V and Promus stents have enjoyed tremendous commercial success. Indeed, Abbott reported that "Xience V became the market-leading drug eluting stent in the U.S. in the fourth quarter of 2008," within just three months of FDA approval. JA9727 at ¶ 225, JA9928 & JA10280. The VDF:HFP coating used in the Xience V stent is an important factor in the clinical success of the Xience V stent, and therefore also in the commercial success of the Xience V and Promus stents. JA9727 at ¶ 225, JA9928 & JA10280. Abbott has represented that "the composition of the polymer coating" in the Xience V stent "is important in overall clinical safety and efficacy outcomes." *Id.* at n.4.

B. The Underlying *Inter Partes* Reexaminations Implicate Objective Evidence of Nonobviousness that Would Be in the Possession of Abbott and Boston Scientific

Cordis sued Abbott and Boston Scientific for infringing the 844 Patent and a related patent (collectively, the "Llanos Patents") covering drug-eluting polymer-coated stents. *Wyeth et al. v. Abbott Labs., et al.*, No. 09-4850 (D.N.J.) (the "Patent Litigation"). In response, the defendants asserted that the patents were invalid because the patented subject matter would have been obvious. They also subsequently initiated the underlying reexaminations (the "Merged

Reexaminations"). JA117-215 & JA784-1178.

The obviousness theories that Abbott and Boston Scientific advanced in the Merged Reexaminations underscore the importance of the objective evidence. When Abbott and Boston Scientific requested *inter partes* reexamination, they argued that Cordis's patent claims were obvious in view of certain combinations of prior art. JA117-215 & JA784-1178. As part of its opposition to these assertions, Cordis submitted declaration testimony of an expert witness, Antonios G. Mikos, Ph.D., who averred that objective evidence supported the nonobviousness of the claims, including, that "[t]he invention of the '844 patent has been copied and adopted by others in the industry, including Abbott Laboratories' Xience V DES and Boston Scientific's Promus DES." JA3763 at ¶ 224; *see also* JA3763-3765. Dr. Mikos also asserted that studies of Xience V demonstrate unexpected thromboresistance and reduced inflammation. JA3764 at ¶ 228; *see also* JA4200-05.

In rebuttal, the Abbott and Boston Scientific criticized this testimony on the basis that "[t]here is no evidence that Dr. Mikos has any first-hand knowledge as to how the Xience V or Promus stents were made" and that "[t]here is nothing to suggest that it was the 'invention' of the 844 Patent that resulted in any sale of the Xience V stent." JA4240-41. Boston Scientific argued to the Patent Office that Dr. Mikos's testimony concerning copying was "legally insufficient" because

Cordis lacked "'internal company documents' or other direct evidence" demonstrating the copying by accused infringers. *Id*.

The Patent Office's non-final office action of January 21, 2011, followed the same reasoning, noting that Cordis had not presented evidence of "how" stents sold by Boston Scientific "were made," but suggested that the Patent Office could be persuaded by additional evidence tending to show "lack of concern for patent property or contempt for the patentee's ability to enforce the patent." JA4642-45.

Abbott similarly endorsed the examiner's reasoning (JA5384), and in the related reexamination proceeding, argued that Dr. Mikos's testimony concerning copying was "fatally flawed" because "[t]here is no evidence that Dr. Mikos has any first-hand knowledge as to how Xience® or Promus® are made" and "Cordis' unsubstantiated copying allegations cannot support the nonobviousness of the Llanos Patent" (JA7829 & JA9471-72). *See also* Comments by Third-Party Requester under 37 C.F.R. § 1.947, In re *Inter Partes* Reexamination of U.S. Patent No. 6,746,773, Reexamination No. 95/000,567 (Aug. 19, 2011) at pp. 45-48.

Notably, Abbott and Boston Scientific did not actually say how their products were made, nor did they mention or explain away the telling fact that a former employee of Johnson & Johnson (Syed Hossainy), who worked contemporaneously with the group that initially developed the claimed invention,

left Johnson & Johnson shortly after and joined Advanced Cardiovascular Systems, now a part of Abbott Laboratories, where he is believed to have been involved in that company's development of the polymer coating used on Xience V and Promus. *See* JA6969-70, JA8033 & JA14056-57.

At the same time that Abbott and Boston Scientific were telling the Patent Office that Cordis lacked the necessary information to support its objective indicia of nonobviousness, they were withholding that very information from the record in the Merged Reexaminations. Thus, Abbott and Boston Scientific have succeeded in keeping the Patent Office record devoid of the key evidence, and then convincing the Examiner and the Board that the objective indicia of nonobviousness offered by Cordis is deficient because of the lack of that key evidence.

C. Cordis Attempted to Use Subpoenas to Obtain the Objective Evidence of Nonobviousness and Cross-Examine the Experts

Because Abbott and Boston Scientific were not obligated to enter into the Patent Office record any objective evidence of nonobviousness that they had, or inform their expert witnesses of the evidence, Cordis sought to make use of the subpoena power provided by 35 U.S.C. § 24 to obtain the evidence and cross-examine the experts on it. The Patent Office's rules — 37 C.F.R. §§ 41.2 & 41.60 — purported to bar subpoenas in *inter partes* reexaminations by deeming such

reexaminations not contested cases. Because these rules hindered Cordis's ability to challenge Abbott's and Boston Scientific's expert witnesses, in February 2011, Cordis filed a complaint in district court alleging that these rules should be set aside as contrary to 35 U.S.C. § 24.[2]

Because Cordis concluded that the Patent Office rules could not legally be applied to it, in October 2011, Cordis joined that issue by filing a petition under 37 C.F.R. § 1.182 in the Merged Reexaminations requesting that the Director clarify the Patent Office's rules as they relate to the service of a subpoena under 35 U.S.C. § 24 in *inter partes* reexaminations. JA6965-71 (the "Petition"). Cordis's Petition requested that the Director confirm that the Patent Office's then-current rules imposed no requirement that parties seeking to enforce subpoenas under § 24 must obtain the Patent Office's prior authorization. The Petition further requested that, to the extent that the Patent Office is of the view that such authorization is required for the enforcement of § 24 subpoenas, the Director grant such authorization so that Cordis may: (i) obtain important information relevant to nonobviousness that is in the possession of the Abbott and Boston Scientific, and (ii) cross-examine expert witnesses whose declarative testimony has been entered

[2] *Cordis Corp. v. Kappos*, No. 1:11-cv-127 (E.D. Va.). The district court dismissed Cordis's complaint because it was filed more than six years after the promulgation of the rules.

into the record by Abbott and Boston Scientific. Cordis submitted subpoenas identifying the documents and testimony along with the Petition, and noted that such subpoenas were in the process of being served. JA6973-6987.

At the same time, Cordis served the subpoenas *duces tecum* and *ad testificandum* on Abbott and Boston Scientific pursuant to 35 U.S.C. § 24. Abbott filed a motion to quash the subpoenas *duces tecum* in the U.S. District Court for the Eastern District of Virginia.[3] In the motion, Abbott did not deny possessing the documents sought by Cordis, nor did Abbott argue that it would be burdensome to produce them. Rather, Abbott argued, *inter alia*, that the subpoenas could not issue because *inter partes* reexaminations were not "contested cases" under 35 U.S.C. § 24. The district court granted Abbott's motion to quash, and Cordis appealed to this Court. *See Abbott Labs. v. Cordis Corp.*, 710 F.3d 1318 (Fed. Cir. 2013).

D. The Patent Office Denied Cordis's Petition, and Cordis Challenged Those Denials in District Court Under the APA

On December 7, 2011, the Patent Office denied Cordis's Petition for the subpoenas in the agency's Original Decision. JA1-9. The stated basis for the Original Decision was that 35 U.S.C. § 24 does not permit discovery in an *inter partes* reexamination proceeding because such proceedings are not "contested

[3] *Abbott Labs. v. Cordis Corp.*, No. 1:11-mc-42 (E.D. Va.).

cases" under the statute. JA5. On January 26, 2012, Cordis brought an action under the APA challenging the Patent Office's Original Decision denying Cordis's petitions.[4] And on March 29, 2012, the district court granted a joint motion to stay the APA Litigation pending the outcome of the appeal to this Court of Abbott's motion to quash in *Abbott v. Cordis*.

This Court ruled in *Abbott v. Cordis* on March 30, 2013, affirming the district court's grant of the motion to quash. In its ruling, however, this Court disagreed with the Patent Office's and Abbott's position that 35 U.S.C. § 24 prohibited subpoenas in *inter partes* reexaminations. Instead, contrary to the Patent Office's litigation position and rules, this Court held that subpoenas are available in any case in which the Director of the Patent Office, by rule, authorizes the taking of a deposition. 710 F.3d at 1322-23.

E. The Patent Office Agreed to Reconsider Its Decision Denying Cordis's Petitions in View of *Abbott v. Cordis*, but After a Year, Still Refused to Address the Petitions on Their Merits

Following the Court's ruling, in May 2013, Cordis and the Patent Office jointly moved in the APA Litigation to remand back to the Patent Office. Because the Court had determined the correct legal backdrop, this remand would be the first occasion for the Patent Office to consider Cordis's request under the correct law.

[4] *Cordis Corp. v. Lee*, No. 12-cv-75 (E.D. Va.) (currently on appeal to this Court in no. 2015-1371) (the "APA Litigation").

The parties noted that the Court "construe[d] the term 'contested case,' as used in section 24, as referring to a proceeding in which the PTO has provided for the taking of depositions for use in that proceeding" and that the Court "h[e]ld that 35 U.S.C. § 24 . . . empowers a district court to issue subpoenas for use in a proceeding before the PTO if the PTO's regulations authorize parties to take depositions for use in that proceeding."[5] Thus, Cordis sought to have the Patent Office reconsider, and the Patent Office agreed to reconsider, the Original Decision in view of this Court's ruling. The district court granted the joint motion to remand.

Pursuant to the agreed-upon remand, in June 2013, Cordis filed Supplemental Submission in support of its earlier Petition in the Merged Reexaminations, requesting that the Director (i) authorize Cordis to cross-examine adverse expert witnesses; (ii) authorize Cordis to obtain the documentary objective evidence of nonobviousness; and (iii) in the alternative, impose upon Abbott and Boston Scientific the same duty of candor to which Cordis is bound. JA14052-14074. In its Supplemental Submission, Cordis argued that the Patent Office's basis for denying the subpoenas — that *inter partes* reexaminations were not contested cases — was rendered invalid by this Court, and that the Patent Office

[5] JA14042 (*Cordis Corp. v. Lee*, No. 12-cv-75, DI16 at 2 (quoting Abbott, 710 F.3d at 1322 & 1328)).

can, and should, provide authorization by exercising its particularized rulemaking authority. JA14053.

Almost a year later, in May 2014, the Patent Office issued a new petition decision. JA10-18 (the "Reconsideration Decision"). In denying the petitions this time, the Patent Office relied on its existing *inter partes* reexamination rules, which do not permit subpoenas to be issued in *inter partes* reexaminations. JA16. The Reconsideration Decision also refused to consider Cordis's situation and its need for the testimony and documents sought. Instead, the Patent Office universally declined to exercise any discretion to make a case-by-case authorization of requests for subpoenas — or impose a duty of candor — because "in a case-by-case adjudication, the Office will only have the input of two parties" and "the Office believes, based on its experience and expertise, that it is impractical and unfair to participants to set rules for *inter partes* reexamination proceedings on an ad hoc basis." JA16-17.

F. Cordis Pursued the APA Litigation Further, but after Three Years of Litigation, the Patent Office Reversed Position on the Finality of Its Decision, and the District Court Agreed

Because the Reconsideration Decision again failed to consider Cordis's need for the objective evidence, Cordis pursued the APA Litigation further, eventually leading to cross-motions for summary judgment. But the district court did not rule on the cross-motions, and instead agreed with the Patent Office's new position that

Cordis's petitions seeking subpoenas were "ancillary to and not dispositive of a final decision" on patentability in the *inter partes* reexaminations.[6] As a result, the district court dismissed the case without prejudice, and did not consider the cross-motions for summary judgment. Cordis timely appealed to this Court, and that appeal is currently pending. No. 2015-1371 (the "APA Appeal").[7]

G. The Examiner Rejected Cordis's Claims and the Board Affirmed the Rejections

The consequences of the Patent Office's studied avoidance of Cordis's requests to complete the record on obviousness became evident during Cordis's appeal of the examiner's rejections and in the Board's ultimate decision.

1. No Prior Art Reference Mentions Using a VDF:HFP Copolymer as a Sustained Release Coating for Any Medical Device, or VDF:HFP in an 85:15 Ratio for Any Medical Device

In the Merged Reexaminations, Abbott and Boston Scientific advanced numerous grounds of rejection (JA124-127 & JA847-864), several of which the examiner adopted (JA3623-24; JA4645-48). As the Board observed, however,

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[6] *Cordis Corp. v. Lee*, No. 12-cv-75, DI70 at 2.

[7] Cordis appealed the district court's dismissal in the APA Litigation because in Cordis's view, the statutory scheme for review of Patent Office petition decisions requires that such decisions be challenged in district court, via the APA. The Patent Office contends that this Court would have jurisdiction to review the Petition Decision in the instant appeal, along with the merits of the Board's decision in the Merged Reexaminations.

these rejections all follow a similar pattern. JA33.

The primary reference said to support the rejection, U.S. Patent No. 5,824,048 ("Tuch") (JA10679-91), relates to polymer-coated stents and teaches that the "polymer chosen must be a polymer that is biocompatible and minimizes irritation to the vessel wall when the stent is implanted" (JA10255 at ¶ 8 & JA10688 at col. 5, ll. 13-15). The reference goes on to list over 50 different polymers and classes of polymers and copolymers, encompassing thousands of different polymers. JA10255 at ¶ 8 & JA10688 at col. 5, ll. 23-54. In spite of this broad disclosure, Tuch makes no mention whatsoever of VDF:HFP copolymers — only VDF homopolymers. JA10255 at ¶ 8 & JA8020. In fact, the patent expresses a clear preference for bioabsorbable polymers (JA10255 at ¶ 9 & JA10688 at col. 5, ll. 16-21), whereas VDF:HFP copolymers are not bioabsorbable. *See* JA9701 at ¶ 55. Consistent with this, all of Tuch's examples are directed to bioabsorbable polymers. JA10255 at ¶ 9 & JA10689-90 at cols. 8-10. Dr. Mikos testified that a person of ordinary skill who read Tuch would have first considered the many other polymers listed in that reference or others in the DES field, or blends of such polymers, rather than looking beyond those references. JA10257 at ¶ 20 & JA10286. Nor does Tuch identify the elasticity of a polymer as a factor that should be considered when deciding whether or not to use it in a drug-containing coating, or suggest the elastomer class of polymers as being useful for a stent coating.

JA10255 at ¶ 10.

The second reference said to support the rejection, U.S. Patent No. 4,816,339 ("Tu") (JA10707-722), does not disclose balloon-expandable stents, but suturable vascular products employing "a multilayered poly(tetrafluoroethylene)/elastomer material . . . where there is improved luminal hydrophobicity, compliance, strength and elasticity." JA10290 & JA10714 at col. 2, ll. 7-11. The multilayered implants that Tu describes may optionally include an outer layer formed by an elastomer, and the elastomers may be selected from a broad list of polymer classes including VDF:HFP. JA10290 & JA10715 at col. 4, ll. 20-40. Tu does not provide an example of an implant in which a VDF:HFP material contacts flowing blood and tissue, nor does Tu mention an 85:15 VDF:HFP ratio.

The third reference, U.S. Patent No. 3,178,399 ("Lo") (JA11105-11) is a 50 year-old patent relating to fluorine-containing polymers in industrial applications such as protective clothing or storage tanks. JA9702-03 at ¶¶ 59-66, JA11106 at col. 1, ll. 23-24 & col. 2, ll. 14-22, JA11108 at col. 6, ll. 61-64. Lo discloses VDF:HFP in an 85:15 ratio, but nowhere mentions its applicability in any biological applications, much less in implantable stents. JA9703 at ¶¶ 64-66.

2. The Board Decision Mapped Cordis's Claim onto Tuch, Tu, and Lo, and Discounted the Objective Evidence of Nonobviousness

The Board decision used Cordis's claim as a roadmap to navigate through the three prior art references. The Board started with Tuch, selecting VDF from among the thousands of individual polymers and polymer classes that the reference discloses, without providing any reason why one of ordinary skill in the art would have focused on VDF. JA38-39.

To the make leap from VDF homopolymers to VDF:HFP copolymers, the Board turned to Tu, positing that one of ordinary skill would have done so "because Tuch's list of polymers is clearly not exhaustive in view of Tuch's description of broad classes of polymers, such as vinyl halide polymers and copolymers, and polyvinylidene halides." JA40. The Board recognized that Tu does not disclose coated stents, but further posited that the Tu polymers would have been "useful for various types of implantable devices." JA42. The Board also found that one of ordinary skill would have looked to Tu because "Tuch teaches elastic polymers are beneficial for coatings in expandable stents," and "Tu's elastomers are elastic." JA43. Tuch, however, does not actually state that elastic polymers are desirable. Rather, the Board made this finding based on the word "resilient" in Tuch's statement that "[t]he inclusion of a polymer in intimate contact with a drug on the stent allows the drug to be retained on the stent in a

resilient matrix during expansion of the stent" (JA35 & 43) and that certain stent *overlayer* materials "which have little elasticity" can crack during deformation (JA35 & 43).

Recognizing that even Tuch and Tu in combination do not disclose VDF:HFP copolymers in an 85:15 ratio, the Board then supposed that one of ordinary skill would have turned to Lo. JA44-45. The Board does not attempt to explain the relevance of Lo to a person of ordinary skill in the medical device field, nor does the Board point to any suggestion that such a person would have consulted literature in Lo's industrial field. Rather, the Board bootstraps its assumption that Tu discloses that VDF:HFP blends are useful in *all* implantable devices, and then further assumes that "the skilled worker would have reasonably consulted Lo" to determine the blend ratio. JA45.

As discussed above, the Board considered, but discounted, the available objective evidence of nonobviousness. First, Cordis argued that the 844 Patent had been copied and adopted by others in the industry, including Abbott and Boston Scientific (JA9727 at ¶ 224 & JA10279-80), but the Board concluded that Cordis lacked "adequate evidence" JA46. Second, Cordis relied upon the remarkable commercial success of Abbott and Boston Scientific's stents (JA9727 at ¶ 225 & JA10280), but the Board found that the success lacked nexus in view of evidence that factors other than the coating contributed to success (JA47-49). Third, Cordis

provided evidence of industry praise of Abbott and Boston Scientific's stents (JA9727-28 at ¶ 226 & JA10280-81), but the Board again found lack of nexus (JA52). Finally, relying on the declaration of Dr. Mikos, Cordis contended that Abbott and Boston Scientific's stents showed surprising thromboresistance and unexpectedly less inflammation (JA9728 at ¶¶ 227-8 & JA10281), but the Board found a lack of nexus in the claims against the closest prior art (JA49-51). The Board did not discuss the fact that the foundational objective evidence it found wanting would be located in the files of Abbott and Boston Scientific, and that they did not make it available to the Patent Office.

In sum, the Board affirmed the examiner's rejection of claims 1-17 and 20-23 of the 844 Patent in view of Tuch, Tu, and Lo. JA52. Cordis timely appealed to this Court. JA14833-14907.

3. The Chief Administrative Patent Judge Declined to Consider Cordis's Petition for Subpoenas

On January 15, 2015, after the district court in the APA Litigation accepted the Patent Office's theory that the Reconsideration Decision should be appealed through the Board and then to this Court, but before the oral hearing before the Board, Cordis petitioned the Chief Administrative Patent Judge of the Board to exercise his authority to afford the subpoenas Cordis had been seeking. JA14532-45. On April 14, 2015, almost two months after the Board's decision on the merits, the Chief Administrative Patent Judge dismissed Cordis's petition seeking

the subpoenas because Cordis "already has received a final agency decision on this matter." JA109-116.

SUMMARY OF THE ARGUMENT

The Obviousness Rejection Is Erroneous on the Record Before the Board. The Board based its obviousness rejections on a combination of references that would have appeared entirely arbitrary to one of ordinary skill in the art at the time of the invention. The Board could only reach its conclusion by using the claims at issue as a road map to find the claimed elements in the prior art. The Board failed to provide any reason why one of ordinary skill would combine the prior art in a way to land on the combination claimed.

The Board combined the vast collection of polymers taught for use in a DES by Tuch (none of which was VDF:HFP) with Tu's disclosure of a VDF:HFP copolymer in a non-DES application. In order to find the particular claimed ratio, it relied on Lo's disclosure of the specifically claimed 85:15 VDF:HFP. JA38-45. Lo does not relate to biological applications at all, much less medical devices or DES.

The Board's logic is rife with errors. First, the Board erred by assuming that a person of ordinary skill would have been dissatisfied with the vast number of polymers disclosed in Tuch. In fact, Tuch teaches away from using VDF:HFP, which is not bioabsorbable, by recommending bioabsorbable polymers.

Second, while close scrutiny of Tuch's extensive disclosure of polymers and polymer classes reveals a *VDF homopolymer* in the list, it is undisputed that Tuch

does not disclose or suggest the use of VDF:HFP. Indeed, there is no teaching in Tuch that the VDF homopolymer had any potential to address the elasticity problem suggested by the Board. The Board erred by not identifying a reason why one of ordinary skill would have focused on VDF as a candidate for further research, much less moved on to a VDF:HFP copolymer.

Third, the Board failed to find motivation to focus on VDF:HFP in Tu, because Tu also presented an extensive list of polymer choices, and again did not highlight VDF:HFP in any way. The Board primarily connected Tuch to Tu by observing that Tuch mentions that a porous layer *over* the drug-eluting polymer can crack during deformation, and by presuming that one of ordinary skill would have extended this elasticity problem to the drug-eluting layer, and addressed this purported issue by using a more elastic polymer (rather than by some other means) and then would have turned to Tu to help solve this problem. But these tenuous connections ignore that a person of ordinary skill would not have been led to explore VDF:HFP, since all of the other polymers that were actually disclosed in the prior art were touted as being effective in a DES. Why would one of ordinary skill focus on VDF:HFP to the exclusion of all others?

Finally, the Board erroneously incorporated the disclosure of Lo into its obviousness theory. The Board relied on Lo for the 85:15 VDF:HFP ratio, but assumed without basis that one of ordinary skill in the DES art would have looked

to Lo's patent on industrial coatings. The only reason to turn to Lo is to find the exact ratio claimed in the 844 patent. This is the definition of hindsight.

The Board's hindsight-driven analysis highlights the crucial importance of the objective evidence of nonobviousness in this dispute. The Board repeatedly ignored Cordis's arguments based on copying, unexpected results, praise, and commercial success because they allegedly lacked sufficient evidentiary foundation. This line of reasoning shows that the Patent Office's denials of Cordis's petitions for subpoenas were prejudicial to Cordis's patent rights.

The Board Decision Should Be Vacated in View of the Arbitrary and Capricious Denials of Cordis's Petitions for Subpoenas. Even without additional evidence, the obviousness rejections should be reversed. Nonetheless, if the Court decides that the current record is sufficient to support the Board's affirmance of the examiner — and that the Court has jurisdiction over Cordis's appeal of the Petition Decision — then the Court should hold that the Decision was unlawful and vacate the Board decision accordingly.

The Patent Office's denials of Cordis's Petitions were arbitrary and capricious under the APA for at least five reasons. First, the Petition Decision relied upon the Patent Office's rules that *inter partes* reexaminations are not contested cases, even though that basis for prohibiting subpoenas was invalidated by this Court in *Abbott v. Cordis*. Second, the Patent Office erroneously refused to

consider Cordis's particular situation and particular need for the information sought in the subpoenas. Third, the Patent Office erred in failing to give weight to the importance of the vital objective evidence of nonobviousness in the context of the Merged Reexaminations. Fourth, the Patent Office erred by refusing Cordis's subpoenas to cross-examine Abbott and Boston Scientific's experts, in spite of the long tradition of affording rights-holders the ability cross-examine adverse witnesses in administrative proceedings. And fifth, if Cordis will not be afforded subpoenas, the Patent Office must at least impose a symmetric duty of candor such that Abbott and Boston Scientific are required, on their own accord, to enter the objective evidence into the reexamination record.

As a final note, the Petition Decision cannot be supported on the ground that the *inter partes* reexamination statute bars subpoenas. The statute operates to embrace the procedures employed during conventional patent examination, but not to exclude other procedures, where appropriate.

Relief requested. Cordis respectfully requests that this Court reverse the Board's decision. In the alternative, this Court should hold that the Patent Office erroneously denied Cordis's petitions for subpoenas, vacate the Board's decision and remand for further proceedings.

ARGUMENT

I. Standard of Review

Obviousness is a legal conclusion based on underlying findings of fact. *In re Sullivan*, 498 F.3d 1345, 1350 (Fed. Cir. 2007). The Board's legal conclusion is, therefore, reviewed *de novo*, while its underlying factual determinations are reviewed for substantial evidence. *Id.* Substantial evidence "requires the reviewing court to ask whether a reasonable person might find that the evidentiary record supports the agency's conclusion." *Id.* (citations omitted).

A court shall set aside agency action found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). "[T]he agency must examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (quoting *Burlington Truck Lines v. United States*, 371 U.S. 156, 168 (1962)). "Normally, an agency rule would be arbitrary and capricious if the agency has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to difference in view or the product of agency expertise." *Id.*

II. The Prior Art Does Not Render the 844 Patent Obvious

The Board improperly relied on hindsight to reconstruct Cordis's claimed inventions in the prior art. The Board, for example, failed to identify any evidence that one of ordinary skill would have recognized any problem with the primary reference, Tuch, or that, even if she had, she would have experimented with the particular copolymer blend that the 844 Patent claims. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 418, 421 (2007) (obviousness findings under 35 U.S.C. § 103(a) require a clearly articulated rationale with a reasonable expectation of success).

"When an obviousness theory is advanced "by 'merely throw[ing] metaphorical darts at a board' in hopes of arriving at a successful result, but 'the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful,' courts should reject 'hindsight claims of obviousness." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation*, 676 F.3d 1063, 1070-71 (Fed. Cir. 2012) (citing *In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009)). Rather, a viable obviousness theory requires that "the possible options skilled artisans would have encountered were 'finite,' 'small,' or 'easily traversed,' and that skilled artisans would have had a reason to select the route that produced the claimed invention." *Id*. at 1073 (citing *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358,

1364 (Fed. Cir. 2008)); *see also Leo Pharm. Prods. v. Rea*, 726 F.3d 1346, 1356-57 (Fed. Cir. 2013) ("[T]he breadth of these choices and the numerous combinations indicate that these disclosures would not have rendered the claimed invention obvious to try.").

A. Tuch Provides No Motivation to Select Polymers Other than Those It Describes

The Board's first error was supposing, without reason, that a person of ordinary skill confronted with the thousands of different polymers embraced by Tuch would have explored other options. Tuch provides an expansive list of polymers for use in its stents, but none of them is a VDF:HFP copolymer. JA10255 at ¶ 8 & JA10688 at col. 5, ll 13-15 and 23-54. Instead, Tuch urges the skilled artisan to use bioabsorbable polymers, and provides examples exclusively using bioabsorbable polymers. JA10255 at ¶ 9 & JA10688 at col. 5, ll. 16-21. In contrast, VDF:HFP is not bioabsorbable. JA9701 at ¶ 55. Although Tuch raises the issue of the elasticity of a porous overlayer disposed on top of the drug-eluting polymer, Tuch never suggests that its drug-eluting polymers lack elasticity or are in any other way deficient. JA10255 at ¶ 10.

As in *Kinetic Concepts*, the record here "is devoid of any reason someone would combine [the cited] references." *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1369 (Fed. Cir. 2012). Where, as here, each device that the references describe "independently operates effectively," a person having ordinary

skill in the art "would have no reason" to combine the references' respective teachings. *Id.* Moreover, even if a person of ordinary skill had recognized the problems with VDF homopolymers that the inventors of the 844 Patent identified (JA10257 at ¶20, *e.g.*, JA238 at col. 5: 4-10 & JA245 col. 19, Example 1), she would not have looked beyond Tuch, but rather would have considered the many other polymers listed in Tuch or other DES references, or blends of those polymers (JA10257 at ¶21).

B. Tuch Provides No Motivation to Select a VDF Homopolymer or VDF:HFP Copolymer

The polymers and polymer classes recited in Tuch embrace a vast genus of potential species. JA10688 at col. 5, ll. 23-54. The magnitude of this "haystack" of candidates becomes even more apparent when one considers how frequently the different polymers mentioned in Tuch had been discussed in the literature. JA8022-23 & 8051-8054. Although Tuch mentions VDF homopolymer, most of the other polymers that Tuch identifies had been referenced in the art much more frequently. *Id*. Indeed, of the approximately 80 polymers that Tuch specifically lists, 52 had been more frequently associated with the terms "drug delivery" and "stent." *Id.* Further, although Tuch discusses the elasticity of a layer disposed over the drug-eluting polymer, Tuch never suggests that the elasticity of the polymer itself is an important characteristic. *Id*; *see also* JA10255 at ¶ 10.

The Board did not even attempt to identify a reason why one of ordinary skill would have dwelled on Tuch's disclosure of VDF, and used it as a lead candidate to develop another DES polymer, much less to develop VDF:HFP. Instead, the Board simply observed that the vast list in Tuch "is a disclosure of each and every one for a stent coating." JA41. The only way the Board could have leapt from this vast and undistinguished list to VDF as a lead candidate is by using Cordis's claim as a guide. This is precisely the kind of hindsight-driven dart-throwing that is forbidden in an obviousness analysis. *Cyclobenzaprine*, 676 F.3d at 1070-71, 1073.

C. Tu Does Not Provide the Motivation to Use VDF:HFP that Tuch Lacks

The Board did not cure the flaws in its obviousness analysis by turning to Tu. Initially, the Board assumed that a person of ordinary skill would have gone from Tuch to Tu, but provided no reason for this other than the plainly inadequate reason that "Tuch's list of polymers is clearly not exhaustive." JA40. As described above, Tuch drew attention to neither VDF nor any property of VDF. As such, there is no reason that one of ordinary skill would have had to search out references (such as Tu) making use of copolymers of VDF. Nor would one of ordinary skill have been drawn to Tu because of its subject matter; rather than stents, Tu is directed to grafts and other suturable devices. JA10174 & JA10292; *see generally* JA10707-722. Nor does Tu itself provide any reason that one of

ordinary skill would have focused on VDF. Instead, Tu (like Tuch) provides a long list of polymer classes, and indeed prefers silicone and copolymers of propylene and tetrafluoroethylene. JA9703-04 at ¶ 16, JA10714 at col. 2, ll. 20-30, JA10715-6 at col. 4:28-39 & col. 4, l. 63- col. 5, l. 7.

The Board's obviousness theory fails to explain why, given the self-contained disclosure of Tuch, a person of ordinary skill would have searched outside the DES literature for still more polymers that had been used in other types of medical devices. The Board states that both Tuch and Tu set forth biocompatible, elastic polymers, but this observation is true of any number of references addressing polymers for biological applications, and does nothing to direct a person of ordinary skill in the art. JA43.

Indeed, even if such a person would have been interested in exploring elastic polymer coatings, the Board does not explain why she would have started with VDF (which is crystalline and, therefore, relatively inelastic) rather than selecting one of the polymers already preferred for DES applications. JA41. Nor does the Board explain why one of ordinary skill would have looked to the vascular grafts of Tu for inspiration, because Tu teaches that in the grafts, the layer possibly containing VDF:HFP should not be in contact with blood, as it would be in a DES: "[i]t is not desired to have the elastomer permeate the poly(tetrafluoroethylene)/

elastomer layer and migrate into the lumen." JA10292 & JA10717 at col. 8, ll. 40-43.

Again, the mere fact that those of ordinary skill in the art *could have* chosen a polymer from Tuch, Tu, or a combination of the two is the makings of a scavenger hunt, not an obviousness theory. *Cyclobenzaprine*, 676 F.3d at 1070-71, 1073; *Leo*, 726 F.3d at 1356-57.

D. A Person of Ordinary Skill Would Have Had No Reason to Consult Lo, Much Less Combine It with Tuch and Tu

As the Board acknowledges, neither Tuch nor Tu discloses the claimed 85:15 ratio of VDF:HFP. Because of this, the Board relies on Lo, a patent that concerns coatings for industrial applications, such as on protective clothing, tanks, and storage vessels. JA9702-03 at ¶¶ 59-66; JA11106 at col. 1, ll. 23-24 & col. 2, ll. 14-22; JA11108 at col. 6, ll. 61-64. The Board does not allege that Lo provides any motivation to combine, or in any way relates to medical devices. Rather, the Board relies upon Lo for its teaching of VDF:HFP properties in the abstract, supposing that one of ordinary skill would have been motivated to consult any reference, no matter how technically unrelated, disclosing elasticity properties of VDF:HFP. JA44-45.

Adding Lo to the prior art combination does not strengthen the Board's supposed motivation to combine, but rather weakens it by expanding the field of search beyond anything tolerated by the case law. *Cyclobenzaprine*, 676 F.3d at

1070-71. Lo is a particularly implausible reference, given its non-analogous technical field as well as the lack of evidence that Lo was ever consulted by persons of ordinary skill in the medical field in the decades it was available. *See Leo*, 726 F.3d 1346 (noting that prior art "was publicly available in the prior art for twenty-two years before the" patent was filed absent any evidence of the purported improvement).

E. The Board Erred in Discounting the Available Objective Evidence and Denying Cordis Access to Subpoenas to Complete the Record

Prior to oral argument before the Board, Cordis petitioned the Chief APJ of the Board for the same relief it had been seeking for years from others within the Patent Office — access to subpoenas on Abbott and Boston Scientific to complete the obviousness record. JA14532-82. The Board panel that heard Cordis's case did not address Cordis's request at oral argument or in its final decision, but the final decision does illustrate the prejudicial effect of the Patent Office's refusal to allow the subpoenas. The Board discounted all of the objective evidence for evidentiary failings: lack of sufficient copying evidence, lack of nexus evidence for commercial success and praise, and lack of sufficient testing information for unexpected results. JA45-52. Because Abbott and Boston Scientific's commercial stents admittedly use the claimed coating, JA14793 at ll. 4-8, all of the evidence the Board found lacking *would be in Abbott and Boston Scientific's possession*.

Thus, when the Chief APJ denied Cordis's petition weeks after the Board decision, he erred for all the reasons described *infra*, Section II., and the decision itself shows why this error was harmful.

III. Even if the Current Record Supports the Board's Obviousness Ruling, the Court Should Vacate the Board Ruling to Allow Cordis to Subpoena Abbott and Boston Scientific for Vital Evidence of Nonobviousness

If the Court determines that it has jurisdiction to review the Petition Decision on appeal, and holds that the Board's affirmance of the rejections was somehow correct on the abbreviated record before it, the Court should then vacate the Board decision and remand so that Cordis can complete the record by subpoenaing Abbott and Boston Scientific for the vital objective evidence of nonobviousness.

The Patent Office's justification has varied over the years, but in spite of Cordis's pleas, and the resources the Patent Office has invested in fighting to avoid Cordis's requests, the Patent Office has never once denied Cordis's requests for subpoenas on the merits — or even addressed Cordis's need for the evidence. The Patent Office's denials, and its failure provide a decision on the merits, are arbitrary and capricious. The evidence is vital, and Cordis should be afforded the subpoenas to introduce the evidence into the record of the pending *inter partes* reexaminations.

A. The Challenged Decisions Were Arbitrary and Capricious

1. The Patent Office's Decision to Adhere to Its Legally Invalid Rules Is Arbitrary and Capricious

In its May 15, 2014, Reconsideration Decision denying Cordis's request for subpoenas, the Patent Office ruled that it would not authorize subpoenas through a particularized rulemaking for two reasons, both of which are legally invalid and therefore arbitrary and capricious.

First, the Patent Office asserted that "[i]t has been the Office's position that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute" and that, "[t]herefore, the Office has not promulgated the regulations as requested." JA17. As an initial matter, the agency's reasoning here contains what is either a non-sequitur or a mischaracterization of Cordis's request. Cordis is seeking the agency's authorization of subpoenas under 35 U.S.C. §§ 23 & 24. Cordis is not seeking "discovery" as that concept is understood in federal district court litigation.

Furthermore, as set out *supra* in Statement of the Case, Section E, the Patent Office's position that the *inter partes* reexamination statute precludes any relief for Cordis was fully presented to this Court by both Abbott and the Patent Office, but the Court did not adopt that position. Rather, the Court adopted the alternative view that the agency maintains "plenary authority" under § 23 over the production of information for purposes of *inter partes* reexaminations. *Abbott v. Cordis*, 710

F. 3d 1318, 1323 (Fed. Cir. 2013). Thus, the Patent Office's first reason for denying Cordis's request — that the agency is legally incapable of doing so because the *inter partes* reexamination statute bars the request — is legally invalid. *Id.*

The Office's alternative ground for denying Cordis's request is that, even if the Office has the authority to grant Cordis's request, it would not do so because it prefers to adhere to its existing rules (which do not permit Cordis subpoenas to obtain the relevant evidence). The agency attempted to justify its adherence to the framework provided by its existing rules on the grounds that it does not want to act through "case-by-case adjudication" and "it is impractical and unfair to participants to set rule for *inter partes* reexamination proceedings on an ad hoc basis." JA17. Normally, of course, agencies can choose to adhere to their existing rules, but not where the reasoning underlying the rules is legally wrong or undermined by subsequent events. *Functional Music, Inc. v. FCC*, 274 F.2d 543, 545 (D.C. Cir. 1958).

This case is similar to *Functional Music*. In applying its rules to a petitioner, the Patent Office has decided to adhere to its pre-existing rules, which establish a *per se* rule forbidding the issuance of any subpoenas in any *inter partes* reexamination. Yet those rules were promulgated based on the agency's legally mistaken view that "[t]he existence of a contested case is a predicate for

authorizing a subpoena under 35 U.S.C. § 24" and that the phrase "contested case" encompassed proceedings such as patent interferences and proceedings with interference-based procedures but not *inter partes* reexaminations. JA13882. In light of this Court's ruling in *Abbott v. Cordis*, that view is now legally insufficient justification for a rulemaking. Under *Abbott v. Cordis*, the phrase "contested case" encompasses any proceedings in which "regulations of the [Patent Office] authorize the parties to take depositions." 710 F.3d at 1320. Thus, where the agency is promulgating new regulations that address the availability of depositions and subpoenas for a new type of proceeding (such as *inter partes* reexaminations), it must provide a reason why it is choosing to include or exclude the new type of proceeding from the category of "contested cases." The Patent Office's 2003 reasoning seems to be based on the incorrect view that *inter partes* reexaminations could not be "contested cases" (because only interference-based proceedings fall within that category) or, alternately, it is completely circular (reasoning that the *inter partes* reexaminations could not be contested cases because no regulation had yet made them contested cases by authorizing depositions under § 23). Either way, the agency's reasoning is legally wrong and cannot support continued application of the rules to bar Cordis's request for subpoenas. *See Massachusetts v. EPA*, 549 U.S. 497, 504 (2007) (holding that the agency has to provide a reasoned explanation for why it was choosing not to regulate).

In sum, a basic principle of administrative law is that "an agency decision cannot be sustained . . . [if] it is based not on the agency's own judgment but on an erroneous view of the law." *Prill v. NLRB*, 755 F.2d 941, 942 (D.C. Cir. 1985). Under this Court's decision in *Abbott v. Cordis*, the Patent Office has the power to classify *inter partes* reexaminations as contested cases and to permit the subpoenas that Cordis seeks. Indeed, Congress has afforded the Patent Office the power to provide for the compulsory processes that are "required" for cases within the agency. 35 U.S.C. § 23. Yet nowhere in the administrative record — neither in its May 2014 orders nor in its earlier rulemaking — has the Patent Office acknowledged that power and provided a reasoned judgment as to why such compulsory process is unnecessary to *inter partes* reexaminations.

2. The Patent Office's Decision to Foreclose Subpoenas Without Regard to the Need for Information in the Proceeding Is Arbitrary and Capricious

An entirely distinct flaw in the Patent Office's *per se* approach to forbidding subpoenas in any *inter partes* reexamination is that the agency has failed even to address — or indeed, even to acknowledge — the relevant considerations in favor of permitting subpoenas in *inter partes* reexaminations. Instead, to the extent the Patent Office has articulated any reasoned basis for its position, it appears be asserting that it will adhere to its existing rules forbidding subpoenas for purposes of administrative convenience and supposed fairness to the parties. Putting to one

side the problem (addressed in Section E, *supra*) that the pre-existing rules also lack a non-arbitrary basis, it is a separate problem than the Patent Office has failed to explain how it balanced interests such as administrative convenience and supposed fairness against the needs of patent holders to obtain highly relevant information from their adversaries.

Reasoned decision-making requires an agency to take into account the relevant factors and to explain why it made the choice it did. Thus, for example, in *Judulang v. Holder*, 132 S. Ct. 476 (2011), the agency defended its immigration policy, *inter alia*, on the grounds that it was administratively simple and thus inexpensive. In its unanimous opinion reversing the agency, the Supreme Court instructed that, while administrative cost may be "an important factor for agencies to consider," nonetheless "cheapness alone cannot save an arbitrary agency policy." *Id.* at 490. Indeed, the Court noted that, if the law were otherwise, an agency could justify "flipping coins" to make administrative decision. *Id.* For an administrative decision to be non-arbitrary, the agency must consider the set of "relevant factors," *id.* at 485 (quoting *Motor Vehicle Mfrs. Assn. of United States, Inc.*, 463 U.S. at 43 (1983)), which means that the agency's reasoning "must be tied, even if loosely, to the purposes of the [relevant statute] or the appropriate operation of the [relevant administrative] system." *Id.* at 485; *see also Michigan v.*

EPA, 135 S.Ct. 2699, 2706-2707 (June 29, 2015) (holding that the agency erred by giving cost "no thought at all" in a cost-benefit analysis).

In this case, as in *Judulang* and *Michigan*, there is simply no indication that the agency gave any consideration to the relevant factors concerning the need for information in *inter partes* reexaminations. Congress created *inter partes* reexaminations as means for evaluating the validity of issued patents, but as the next section of this brief demonstrates, an evaluation of obviousness requires information concerning the objective indicia. In its administrative submissions, Cordis placed these precedents before the agency, and yet nowhere in its decisions does the Patent Office provide any hint that it considered the need for this sort of information and the consequences of forbidding any compulsory process to obtain it. Under *Judulang* and *Michigan*, that failure of reasoning is fatal to the agency's decision. *see also American Horse Protection Assn. v. Lyng*, 812 F. 2d 1 (D.C. Cir. 1987) (overturning agency decision because a "conclusory statement lack[ing] substance" was "insufficient to assure a reviewing court that the agency's refusal to act was the product of reasoned decisionmaking").

The Patent Office could not have rationally concluded that it did not have to consider Cordis's individual situation. The Patent Office's stated bases for refusing to consider Cordis's situation were that: (1) "[i]t has been the Office's position" that subpoenas are not permitted; (2) the agency would only have the

input of two parties; and (3) "it is impractical and unfair to participants to set rules for *inter partes* reexamination proceedings on an ad hoc basis." JA25. The first of these reasons is legally invalid, as explained above. The other two reasons are entirely conclusory and self-serving.

The Patent Office has never explained why it would need third-party input to decide whether to provide subpoenas in *inter partes* reexaminations involving only Cordis, Abbott, and Boston Scientific. And the Patent Office's statement that it would be "impractical and unfair" to address Cordis's situation individually is similarly conclusory. It is not clear how Cordis's proposal is any different from what happens in any other Patent Office proceeding. Specific to seeking documents, it is commonplace in *inter partes* review for individual parties to seek relief, provide their justification, and then obtain a reasoned decision from the Patent Office. *See, e.g.*, 77 Fed. Reg. 48612, 48622 (Aug. 14, 2012); *Garmin International, Inc. v. Cuozzo Speed Technologies LLC*, IPR2012-00001, Paper No. 26 (P.T.A.B. March 5, 2013). Thus, it is especially difficult to understand or accept the agency's offhand reference to practicality and fairness as a basis for its decisions, considering that it has already demonstrated that it is capable of administering such requests on a case-by-case basis.

Finally, even if the considerations advanced by the Patent Office are legitimate factors that the agency can take into account, the agency's decisions

below are still arbitrary and capricious because the agency failed to consider how those factors should be balanced against the need for subpoenas to obtain objective indicia of nonobviousness. *See Michigan*, 135 S. Ct. at 2706-07.

3. The Patent Office's Decision to Refuse Subpoenas Necessary to Obtain Objective Evidence of Nonobviousness is Arbitrary, Capricious, and Contrary to Law

The subpoenas Cordis seeks go to the heart of the only question at issue in the *inter partes* reexaminations: were Cordis's patent claims obvious to a person of ordinary skill at the time they were filed? As this Court has repeatedly held, it is reversible error to ignore the objective evidence of nonobviousness. Yet the Patent Office refused to allow Cordis to obtain this crucial documentary evidence from Abbott and refused to allow Cordis to cross-examine Abbott's expert obviousness witness about this evidence. And the Patent Office made this refusal without ever acknowledging the importance of this evidence or explaining how or why the evidence would not be necessary in the Merged Reexaminations.

Any process that threatens to hold patent claims invalid for obviousness must include an adequate mechanism to bring objective evidence into the record and factor it into the determination. Indeed, the objective evidence "must" be considered. *Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372, 1378 (Fed. Cir. 2012); *In re Kao*, 639 F.3d 1057, 1067 (Fed. Cir. 2011) (reversing the decision of the BPAI and noting that "it is error not to consider" objective evidence). Often, it is

"the most probative and cogent evidence of nonobviousness in the record." *Ortho-McNeil Pharm. v. Mylan Labs.*, Inc., 520 F.3d 1358, 1365 (Fed. Cir. 2008). This is because the obviousness analysis is susceptible to hindsight bias, and the objective evidence is a "built-in protection" that "can help to place a scientific advance in the proper temporal and technical perspective when tested years later for obviousness against charges of making only a minor incremental improvement." *Mintz*, 679 F.3d at 1378. Objective evidence is paramount where, as in these *inter partes* reexaminations, there is a battle of experts. *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1370-71 (Fed. Cir. 2012) ("The objective indicia of nonobviousness serve a particularly important role in a case, like this one, where there is a battle of scientific experts regarding the obviousness of the invention. In such a case, the objective indicia provide an unbiased indication regarding the credibility of that evidence.").

This Court has repeatedly reversed decisions of the Patent Office for failure to properly consider or weigh the objective evidence of nonobviousness. *E.g., Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346 (Fed. Cir. 2013); *Rambus Inc. v. Rea*, 731 F.3d 1248 (Fed. Cir. 2013); *Institut Pasteur v. Focarino*, 738 F.3d 1337 (Fed. Cir. 2013); *In re Kao*, 639 F.3d 1057 (Fed. Cir. 2011). The lesson of these decisions cannot be ignored: a proper and fair determination of obviousness requires full consideration of the objective evidence of nonobviousness.

These Merged Reexaminations present the quintessential dispute that requires objective evidence to resolve: obviousness is the only issue, and each party has presented expert declaration testimony supporting its views. Indeed, to drive the point home, Abbott and Boston Scientific challenged Cordis's views on copying — one type of objective evidence of nonobviousness — because Cordis's expert lacked first-hand knowledge of the copying. JA4240-41 & JA7829. But this is precisely why the subpoenas are warranted — to obtain the documentary evidence itself, and to confront Abbott's expert and Boston Scientific's expert with that evidence.

In spite of the lengthy obviousness dispute on the record in the Merged Reexaminations, and Cordis's requests to obtain the information specifically relevant to this dispute, the Patent Office did not address the issue in denying Cordis's subpoenas. In its original denial of December 2011, the Patent Office based its decision exclusively on its erroneous interpretation of § 24. JA4-8. And in its denial of May 2014, the agency simply revised its blanket denial, again failing to address either Cordis's need for the evidence or the importance of objective evidence to a nonobviousness analysis. JA10-18. There is no way that the Patent Office could have reached a non-arbitrary decision to block Cordis's access to subpoenas on objective evidence of nonobviousness without even

considering the importance of that evidence. The agency's denial of the subpoenas was arbitrary and capricious for this reason. *Motor Vehicle Mfrs.*, 463 U.S. at 43.

4. The Patent Office's Decision to Refuse Subpoenas Necessary to Cross-Examine Adverse Expert Witnesses Was Arbitrary, Capricious, and Contrary to Law

The Patent Office's decision denying Cordis's subpoenas was also arbitrary and capricious because it prevents Cordis from cross-examining the third-party requester's experts. Not only does this allow those experts to provide unchallenged testimony, but it also allows them to testify in studied ignorance of the objective evidence of nonobviousness, which Abbott and Boston Scientific had no obligation to provide to the experts. The combination of the lack of subpoenas and the asymmetrical duty of disclosure at the Patent Office works considerable prejudice against Cordis, which can do little but disagree with the unfounded conclusions of its opponents' experts. In its decisions, the Patent Office failed to address this unfairness, or even consider Cordis's need for cross-examination in any general or particular way. *See* JA1-26 & JA109-116.

Because *inter partes* reexamination proceedings can deprive the patent owner of its previously awarded patent rights, such proceedings must afford the owner the protections of due process, especially the ability to confront and cross-examine a challenger's expert witnesses. *See Goldberg v. Kelly*, 397 U.S. 254, 262 (1970) (holding that the constraints of due process apply to any administrative

process "that adjudicates important rights"); *Fla. Prepaid Postsecondary Educ. Expense Bd v. College Sav. Bank*, 527 U.S. 627, 642 (1999); *In re Enhanced Sec. Res., LLC*, 739 F.3d 1347, 1362 (Fed. Cir. 2014) (O'Malley, J., dissenting) ("While due process considerations frequently focus on notice and hearing, this court has acknowledged that additional procedures may be mandated by due process when the PTO acts.").

The extent of due process rights in the administrative context is governed by the balancing test set forth in *Mathews v. Eldridge*, 424 U.S. 319, 335 (1976), which requires consideration of three factors. There is little doubt that Cordis's private interest affected by the Patent Office's decision is large. And long-standing precedent holds that due process[8] requires that participants in an administrative process be given some opportunity to cross-examine and subpoena experts who submit reports in the administrative process. *See, e.g.*, *Lidy v. Sullivan*, 911 F.2d

[8] In *Abbott v. Cordis*, the Court held that the exclusion of compulsory process in *inter partes* reexaminations did not raise a significant constitutional problem "under the facts of this case." *Id.* at 1323. Under the facts of that case, a constitutional problem did not arise from the exclusion of compulsory process because the Patent Office retained its ability to authorize any necessary subpoenas where it determined under section 23 that the production of evidence was necessary or appropriate for the proceeding. Indeed, the court specifically noted that the agency retains authority over "the production of evidence through section 23" of the Patent Act. *Id.* Limited as it was to the "facts of this case," the ruling in *Abbott v. Cordis* does not resolve the constitutional issue presented here, which deals with the necessity for certain forms of evidence to the fair resolution of these *inter partes* reexaminations, and the need for the Patent Office to actually exercise the authority that the Court recognized.

1075, 1077 (5th Cir. 1990); *see generally* Victor G. Rosenblum, *The Right to Cross-Examine Physicians in Social Security Disability Cases*, 26 Fla. St. U. L. Rev. 1049 (1999) (summarizing the relevant caselaw). As Judge Moore noted in her concurrence in *Gambill v. Shinseki*, 576 F. 3d 1307, 1326 (Fed. Cir. 2009) (Moore, J., concurring), "most of the circuits require an absolute right to cross-examination" even in "the decidedly informal and non-adversarial nature of the social security disability system," and all circuits recognize a right to some compulsory processes to challenge expert witnesses (either by cross-examination or by compulsory interrogatories).

Finally, the third factor in the *Mathews* analysis requires assessment of the government's interest, especially the government's interest in avoiding undue administrative burdens. Although permitting Cordis to depose the third-party requester's experts here will entail some modest additional administrative burdens, there is no reason to suspect that these will be especially heavy. Such depositions are ubiquitous in *inter partes* review proceedings (*see* 37 C.F.R. § 42.52-53), and those proceedings are completed significantly more quickly than *inter partes* reexaminations. Especially considering the high stakes here, and the time-honored right to cross-examine adverse witnesses, any slight administrative burden should not stand in the way of rules allowing such cross-examination.

The combination of the fundamental right to cross-examine adverse witnesses — and the particular need to do so here to help resolve the battle of experts on the issue of obviousness — renders the Patent Office's denial of the subpoenas *ad testificandum* arbitrary and capricious. The Patent Office compounded this error and revealed the arbitrariness of their decision by failing to consider or weigh these important needs. This failure, too, was arbitrary and capricious.

5. The Patent Office's Decision to Maintain an Asymmetric Duty of Candor in These Merged Reexaminations Is Arbitrary and Capricious

Cordis presented the Patent Office with a simple alternative to affording Cordis access to the subpoenas: imposing a duty of disclosure on Abbott and Boston Scientific mirroring that already imposed on Cordis. Again, the Patent Office denied this request without considering its merits. And again, both the agency's denial and its baseless reasoning were arbitrary and capricious.

Under the current Patent Office rules, an accused infringer can get the upper hand on a patent owner by initiating an *inter partes* reexamination and obtaining a stay of the litigation. Sheltered by these rules, Abbott and Boston Scientific have been trying to prove obviousness in the absence of the damaging objective evidence of nonobviousness. They have done this simply by contending that the relevant documents are confidential and refusing to allow Cordis to submit them to

the Patent Office. And unlike Cordis, there is no affirmative duty of candor for third-party requesters in *inter partes* reexaminations. 37 C.F.R. § 1.933. Instead, third-party requesters like Abbott and Boston Scientific are subject only to the general duty required under 37 C.F.R. § 11.18, which includes no affirmative obligation of disclosure.

The Patent Office should not continue to give Abbott and Boston Scientific the ability to hide crucial evidence of nonbviousness, and instead should impose upon them the same duty of candor that Cordis faces, *i.e.*, the third-party requesters should have to disclose information tending to prove patentability and information that refutes, or is inconsistent with, a position taken by them, including objective evidence of nonobviousness. There is no apparent reason not to impose this duty on third party requesters, and indeed it is imposed by the rules that apply to *inter partes* review. 37 C.F.R. § 42.11. Such a rule has the particular advantage of imposing no administrative burden on the Patent Office. Furthermore, introducing this crucial information (such as objective evidence of nonobviousness) into the *inter partes* reexamination record will improve the accuracy of the adjudication, which benefits the public and should be the Patent Office's highest goal.

In spite of the compelling reasons to impose the duty of candor on Abbott and Boston Scientific in these proceedings, especially where Cordis cannot access subpoenas, the Patent Office summarily denied Cordis's request without even

considering the merits of the request. This denial, and its reasoning, are arbitrary and capricious. *Motor Vehicle Mfrs.*, 463 U.S. at 43.

B. The *Inter Partes* Reexamination Statute Does Not Prohibit the Subpoenas Cordis Seeks

The Patent Office and Abbott have suggested that the language of the *inter partes* reexamination statute, 35 U.S.C. § 314, supports the Patent Office's decisions by prohibiting subpoenas. To the contrary, not only does § 314 not prohibit subpoenas, but the Patent Office's own practices and procedures also demonstrate that subpoenas would be entirely appropriate in *inter partes* reexaminations.

1. Subpoenas Are Fully Consistent with the Current *Inter Partes* Reexamination Process

a) The Relevant Statute Includes the Procedures of Initial Examination and Does not Exclude Additional Procedures

Section 314(a) does not purport to prescribe any comprehensive and exclusive set of procedures for *inter partes* reexamination, much less prohibit the subpoenas Cordis seeks. The statute adds nothing at all to this Court's holding that § 24 subpoenas are available wherever the Patent Office allows depositions. Rather, the plain language of the statute — "reexamination shall be conducted according to the procedures established for initial examination under the provisions of sections 132 and 133" — merely requires that reexamination follow the procedures for initial examination set forth in two sections of the Patent Act —

§§ 132 and 133. Those sections, in turn, provide only a few guideposts on rejections, amendments, deadlines, and regulatory power. §§ 132 &133.

Sections 132, 133, & 314 do not prohibit procedures other than those listed in §§ 132 & 133 in *inter partes* reexaminations. Rather, *inter partes* reexaminations are replete with procedural rules that differ from initial examination. Representative of these rules are the ones that provide for: no interviews with the examiner, unlike initial examination (*compare* MPEP § 2685 with MPEP § 713); three examiners from the Central Reexamination Unit instead of a single examiner (MPEP § 2671.03); a panel review at each stage of examination (*id.*); amendments not enlarging the scope of a claim (MPEP § 2658); and so on.

These examples make plain that *inter partes* reexaminations incorporate any number of procedures that are not used in initial examination. Indeed, subpoenas have an even stronger provenance than these other procedures, because the authority for subpoenas in *inter partes* reexaminations derives from a specific statute (*i.e.*, § 24) that § 314 did not repeal or modify.

b) Subpoenas Are Entirely Compatible with, and Appropriate for, *Inter Partes* Reexamination

Cordis's subpoenas for specific documentary evidence on the question of nonobviousness do not work against the purposes of *inter partes* reexaminations. For example, the requirement that *inter partes* reexaminations proceed with

"special dispatch" is not inconsistent with the subpoenas Cordis seeks. Nor does the recent replacement of *inter partes* reexaminations with *inter partes* review. To the contrary, in the new review proceedings, the Patent Office has been proving Cordis's point that subpoenas are fully compatible with a tight schedule. The rules for the new *inter partes* review proceedings "are to be construed so as to ensure the just, speedy, and inexpensive resolution" of the proceeding. Office Patent Trial Practice Guide, 77 Fed. Reg. 48756, 48758 (Aug. 14, 2012). In accordance with this speedy resolution, the Patent Office provided a representative timeline for *inter partes* review that is limited to no more than 18 months total, and 12 months from petition decision until final decision, including periods as brief as one month for "patent owner discovery." *Id.* at 48757.[9] This schedule, which the Patent Office has implemented successfully,[10] is several times faster than the "special

[9] Recently, the Board accelerated the already quick standard scheduling order for *inter partes* reviews, further showing that depositions and the like are entirely feasible on schedules much shorter than that for an *inter partes* reexamination. *See* Mckeown, Scott, "PTAB Accelerates Post Grant Trial Schedules by Two Months," Patents Post-Grant, available at http://www.patentspostgrant.com/ptab-switches-to-faster-default-docket (last accessed Aug. 17, 2015).

[10] *See* AIA Trial Proceeding Statistics, available at http://www.uspto.gov/sites/default/files/ip/boards/bpai/stats/aia_trial_proceedings.pdf (last accessed Aug. 17, 2015).

dispatch" of *inter partes* reexaminations,[11] and demonstrates that there is no danger of subpoenas slowing down *inter partes* reexaminations.[12] Moreover, the procedures for *inter partes* review accommodate far more than compelled testimony under § 24, extending to various routine and additional discovery. 77 Fed. Reg. at 48761-62.

2. This Court's *Abbott v. Cordis* Decision Significantly Undermined the Patent Office's Reasoning

The Patent Office's arguments about § 314 were not sustained by *Abbott v. Cordis*. In that case, Cordis appealed the district court's grant of Abbott's motion to quash, arguing that because § 24 affords subpoenas in "contested cases" (and because *inter partes* reexaminations are adversarial proceedings having well-accepted criteria of contested cases) subpoenas are automatically available in *inter partes* reexaminations. Abbott and the Patent Office disagreed, with each offering different definitions of "contested case" that would exclude *inter partes* reexaminations, and with each pointing to § 314 as further rendering subpoenas

[11] Compare the 12-month *inter partes review* timeline to the 34-47 month "special dispatch" of *inter partes* reexaminations. *See* Reexaminations – FY 2014 available at http://www.uspto.gov/sites/default/files/patents/stats/Reexamination_operational_statistic_F_14_Q3.pdf (last accessed Aug. 17, 2015).

[12] In spite of "special dispatch," the Patent Office will stay an *inter partes* reexamination for good cause, such as judicial efficiency. *Samsung Elecs. v. Fractus*, IPR2014-8, 11,12,13, Paper No. 14, (P.T.A.B. Nov. 12, 2013).

unavailable. Their argument was, at its essence, that the Patent Office lacked discretion and could *never* allow subpoenas in *inter partes* reexaminations.

On appeal, this Court considered the issue of "whether 35 U.S.C. § 24 empowers a district court to issue a subpoena for use in an *inter partes* reexamination turns on whether an *inter partes* reexamination is a 'contested case' within the meaning of section 24." 710 F.3d at 1320. In answering that question, the Court specifically rejected the parties' "dueling laundry lists of the attributes of a 'contested case'" and held that the Patent Office "maintains 'plenary authority' over the production of evidence through section 23." *Id.* at 1322. Thus, rather than address what § 314 does or does not allow, the Court recognized the Patent Office's authority, holding that "section 24 only empowers district courts to issue subpoenas in proceedings for which the PTO has authorized parties to present evidence by means of depositions." *Id.* at 1326. This is a radical change to the landscape as the Patent Office understood it prior to this Court's decision. Whereas the Patent Office had thought itself barred from providing the subpoenas, this Court recognized that subpoenas may be afforded.

The Patent Office explicitly recognized this change in the law. After *Abbott v. Cordis* was decided, the Patent Office agreed to reconsider its petition decisions in view of this Court's ruling, and recognized that "[g]ood cause exists for such a remand because the issues presented by this litigation might be entirely resolved by

the USPTO's reconsideration of its previous decisions, thus conserving judicial resources and avoiding any further unnecessary litigation." JA14042. And following that remand, the Patent Office accepted briefing from Cordis and Abbott, and took nearly a full *year* to reach its revised decision. Thus, this Court's ruling at a minimum casts considerable doubt on a harsh interpretation of § 314 by recognizing the Patent Office's plenary authority.

CONCLUSION

For the reasons stated, Cordis respectfully requests that this Court reverse the Board's decision. In the alternative, this Court should hold that the Patent Office acted unlawfully in denying Cordis's petitions for subpoenas, vacate the Board's decision, and remand for further proceedings.

Date: August 17, 2015

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ADDENDUM

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/000,542 95/000552	04/15/2010	7,591,844 B2	CRDS-0116	8264

45511 7590 12/07/2011

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED: 12/07/2011

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patents and Trademark Office
P.O.Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

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THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS

FROMMER LAWRENCE & HAUG
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Date: 12-7-11

Transmittal of Communication to Third Party Requester
Inter Partes Reexamination

REEXAMINATION CONTROL NO. : 95000542 95/000552
PATENT NO. : 7591844
TECHNOLOGY CENTER : 3999
ART UNIT : 3993

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above identified Reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the inter partes reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an ex parte reexamination has been merged with the inter partes reexamination, no responsive submission by any ex parte third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the Central Reexamination Unit at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

PTOL-2070(Rev.07-04)

United States Patent and Trademark Office

Commissioner for Patents
United States Patent and Trademark Office
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Alexandria, VA 22313-1450
www.uspto.gov

MAILED (For Patent Owner)

DEC 07 2011

CENTRAL REEXAMINATION UNIT

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Inter Partes Reexamination Proceeding
Control No. 95/000,542
Filed: April 15, 2010
For: U.S. Patent No.: 7,591,844

Inter Partes Reexamination Proceeding
Control No. 95/000,552
Filed: June 14, 2010
For: U.S. Patent No. 7,591,844

DECISION DENYING PETITION

This decision addresses the following:

1. The October 7, 2011 patent owner petition entitled "Petition Under 37 C.F.R. § 1.182", filed on October 7, 2011" (the October 7, 2011 patent owner petition under 1.182);

2. The November 2, 2011 opposition petition by the *inter partes* '552 requester entitled "Requester Abbott's Petition to Respond to Patent Owner's October 7, 2011 Petition Under 37 C.F.R. § 1.182 Seeking Unprecedented Discovery in *Inter Partes* Reexamination Proceedings" (the November 2, 2011 opposition by the *inter partes* '552 requester); and

3. The November 3, 2011 opposition petition by the *inter partes* '542 requester entitled "Third Part [*sic*] Requester Boston Scientific's Opposition Under 37 C.F.R. § 1.182 To Patent Owner's Petition for Discovery" (the November 3, 2011 opposition by the *inter partes* '542 requester).

The October 7, 2011 patent owner petition under 37 CFR 1.182, the November 2, 2011 opposition by the *inter partes* '552 requester, the November 3, 2011 opposition by the *inter partes* '542 requester, and the record as a whole, are before the Office of Patent Legal Administration for consideration.

SUMMARY

Patent owner's October 7, 2011 petition under 37 CFR 1.182 is **denied**. Discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute, or by any regulation governing *inter partes* reexamination proceedings.

Patent owner's October 7, 2011 alternative petition under 37 CFR 1.182, requesting the Office to authorize discovery under 35 U.S.C. 24 in the present merged proceeding, is **denied**.

This decision is designated as a final agency action under 5 U.S.C. § 704.

DECISION

The patent owner requests that the Office "clarify" its rules as they relate to the service of a subpoena under 35 U.S.C. 24 in *inter partes* reexamination proceedings. Specifically, the patent owner requests that the Office "confirm that its current rules impose no requirement that parties seeking to enforce subpoenas under § 24 must obtain the Office's authorization". Alternatively, the patent owner requests:

> if the Office takes the position that such authorization is required for the enforcement of § 24 subpoenas, . . . that the Office grant such authorization so that Patent Owner may (i) obtain important information relevant to nonobviousness that is in the possession of the Third Party Requesters (TPRs) in these merged reexaminations, and (ii) cross-examine expert witnesses whose declarative testimony has been entered into the record of these consolidated inter partes reexaminations by TPRs.

35 U.S.C. 24 provides, in pertinent part (emphasis added):

> The clerk of any United States court for the district wherein testimony is to be taken for use *in any contested case in the Patent and Trademark Office*, shall, upon the application of any party thereto, issue a subpoena for any witness residing or being within such district, commanding him to appear and testify before an officer in such district authorized to take depositions and affidavits, at the time and place stated in the subpoena. The provisions of the Federal Rules of Civil Procedure relating to the attendance of witnesses and to the production of documents and things shall apply to contested cases in the Patent and Trademark Office....

The *inter partes* reexamination statute, however, does not authorize discovery in *inter partes* reexamination proceedings. 35 U.S.C. 24 is not applicable to *inter partes* reexamination proceedings.

Optional *inter partes* reexamination was enacted in the American Inventors Protection Act of 1999 (the AIPA). See Public Law 106-113, 113 Stat. 1501, 1501A-552 through 1501A-591 (1999), codified at 35 U.S.C. 311–318. 35 U.S.C. 311–318 provide for the filing of a request for *inter partes* reexamination, the Office's decision on such a request, an examination stage including Office actions on the merits, patent owner responses to the Office actions, and third-party requester comments (where patent owner responds) addressing issues raised by the Office action and/or the patent owner's response, an appeal stage, and the issuance of a certificate at the

conclusion of the proceedings. The AIPA provided that the patent owner in an *inter partes* reexamination could appeal a decision of the Board of Patent Appeals and Interferences (BPAI) adverse to patent owner to the United States Court of Appeals for the Federal Circuit (Federal Circuit). However, as originally enacted, the AIPA did not permit a third party requester of the *inter partes* reexamination to appeal an adverse decision of the BPAI to the Federal Circuit, and did not provide for third-party-requester participation in an appeal taken by the patent owner to the Federal Circuit. Subsequently, the *21st Century Department of Justice Appropriations Authorization Act* (*see* Pub. L. 107-273, 116 Stat. 1758, 1899-1906 (2002)) via section 13106, granted the third party requester the rights to (a) appeal an adverse decision of the BPAI to the Federal Circuit (in which appeal the patent owner may participate), and (b) be a party to a patent owner appeal to the Federal Circuit. **Such is the extent of third party participation in an *inter partes* reexamination proceeding, as provided by the 1999 and 2002 enactments.**

35 U.S.C. 314 prescribes the procedure for the conduct of *inter partes* reexamination proceedings. 35 U.S.C. 314(a) provides, in pertinent part:

> Except as otherwise provided in this section, reexamination shall be conducted according to the procedures established for initial examination under the provisions of sections 132 and 133.

35 U.S.C. 132 and 133, which govern initial examination, do not provide for a discovery practice. In addition, the initial examination of a patent application is not a "contested case in the Patent and Trademark Office" within the meaning of 35 U.S.C. 24. 35 U.S.C. 132 and 133 address initial examination, and not adjudication, and accordingly do not provide any basis for the authorization of discovery under 35 U.S.C. 24. Moreover, 35 U.S.C. 305, which includes corresponding provisions governing *ex parte* reexamination, similarly specifies that *ex parte* reexamination "will be conducted according to the procedures established for initial examination under the provisions of sections 132 and 133." The fact that the same language is used to describe the conduct of *ex parte* reexamination proceedings, which do not provide for discovery, suggests that discovery practice is not within the scope of any reexamination proceeding, whether *inter partes* or *ex parte*. *Cf. Rules to Implement Optional Inter Partes Reexamination Proceeding*, 65 Fed. Reg. 76,756, 76,763 (December 7, 2000) (final rule) ("In a very real sense, the intent of reexamination is to start over and reexamine the patent and examine new and amended claims *as they would have been examined in the original application of the patent.*") (emphasis added).

35 U.S.C. 314(b) provides for service of parties and for the submission of written comments by the third party requester after a patent owner response during the examination stage. Third party requester's written comments must be filed within thirty days of the date of service of patent owner's response. There is no authorization for discovery. Furthermore, as argued by the third party requester in the '542 proceeding,[1] it would be impracticable, if not impossible, for the parties to conduct discovery, for the court to resolve any discovery disputes, and for the third party requester to prepare and submit its written comments within the thirty-day period set by statute. The fact that Congress required the third party requester to file written comments within

[1] See the November 3, 2011 opposition by the third party requester, Boston Scientific, of *inter partes* reexamination proceeding 95/000,542.

a thirty-day period provides evidence that Congress did not intend to authorize discovery practice in *inter partes* reexamination proceedings.

Both 35 U.S.C. § 314(c), which governs *inter partes* reexamination, and 35 U.S.C. § 305, which governs *ex parte* reexamination, provide that reexamination in *inter partes* reexamination and in *ex parte* reexamination proceedings, respectively, will be conducted with "special dispatch" within the Office. Neither the statute nor the regulations define special dispatch; however, in *Ethicon v. Quigg*, 849 F.2d 1422, 7 USPQ2d 1152 (Fed. Cir. 1988), the Federal Circuit explained:

> "Special dispatch" is not defined by statute. . . . According to Webster's New World Dictionary, special means distinctive, unique, exceptional or extraordinary, and dispatch means to finish quickly or promptly. Consequently, the ordinary, contemporary and common meaning of special dispatch envisions some type of unique, extraordinary or accelerated movement. In fact, the PTO itself has interpreted special dispatch to require that 'reexamination proceedings will be "special" through their pendency' in the office and provides for an accelerated schedule. MPEP § 2261.
>
> *Ethicon*, 849 F.2d at 1426.

Any provision for discovery would necessarily prolong proceedings before the Office. If Congress had intended for discovery to be permitted in inter partes reexamination proceedings, rather than in ex parte reexamination proceedings, Congress would have expressly provided for such a practice, and it would have circumscribed the discovery in a manner consistent with the statutory requirement for "special dispatch." Thus, the statutory requirement for special dispatch clearly provides evidence that Congress did not contemplate discovery for *inter partes* reexamination proceedings. Regarding the sole exception to the "special dispatch" requirement, i.e., a finding of "good cause" by the Director, the Office has not authorized an exception to the "special dispatch" provision for the purposes of permitting discovery, and is not authorized to do so, given the above-discussed provisions of 35 U.S.C. 314(a).

The above interpretation of the *inter partes* reexamination provisions is consistent with their legislative history. The legislative history makes no mention of discovery, and consistently expresses a concern for providing a low-cost, efficient alternative to litigation, in which a third party requester has the ability to participate by submitting comments, in writing, to the examiner, in response to arguments made by the patentee. See, e.g., 145 Cong. Rec. H6944 (Aug. 3, 1999) (Statement of Rep. Rohrabacher) (indicating that the AIPA was intended to create a proceeding like *ex parte* reexamination which did "not subject the patent to any greater challenge in scope than currently exists today" but "merely allows a reexam requestor the option to further explain why a particular patent should not have been granted"); H.R. Rep. No. 106-287, 106th Cong., 1st Sess. 31, (1999) (Submitted by Rep. Coble) ("The existing patent reexamination system is an ineffective means for bringing relevant prior art unavailable to examiners during their search to the attention of the PTO due to the ex parte nature of the proceeding.");145 Cong. Rec. S14720, (Nov. 17, 1999) (Statement of Senator Lott) ("Subtitle F is intended to reduce expensive patent litigation in U.S. district courts by giving third-party requesters, in addition to the existing *ex parte* reexamination in Chapter 30 of title 35, the option of *inter partes* reexamination proceedings in the USPTO. Congress enacted legislation to authorize *ex parte* reexamination of

patents in the USPTO in 1980, but such reexamination has been used infrequently since a third party who requests reexamination cannot participate at all after initiating the proceedings. Numerous witnesses have suggested that the volume of lawsuits in district courts will be reduced if third parties can be encouraged to use reexamination by giving them an opportunity to argue their case for patent invalidity in the USPTO. Subtitle F provides that opportunity as an option to the existing *ex parte* reexamination proceedings.").

The Office has implicitly understood that the *inter partes* reexamination provisions do not authorize discovery. In response to a reporting requirement of the AIPA (*see* AIPA, Pub. L. 106-113, 1501A-571, § 4606 (1999)), the Office conducted a "round table meeting" to receive views on the effectiveness and possible improvement of *inter partes* reexamination and then drafted a report to Congress. The report points out that "the lack of such procedural mechanisms as discovery and cross-examination that would be available in litigation has apparently resulted in challengers being unwilling to invoke inter partes reexamination and risk its estoppel effect." United States Patent And Trademark Office Report To Congress On Inter Partes Reexamination (2004) (available at http://www.uspto.gov/web/offices/dcom/olia/reports/reexam_report.htm), at 4; *see also* Transcript of February 17, 2004 Roundtable Meeting (available at http://www.uspto.gov/web/offices/pac/dapp/opla/comments/reexamproceed/round_tbl_transcript.pdf) at 20-21 (discussing the lack of discovery in *inter partes* reexamination). The report contrasts *inter partes* reexamination to a proposed "post-grant review process," in which "[c]losely controlled discovery and cross-examination would be available in the review, upon the challenger's presenting sufficient grounds that one or more of the patent claims are unpatentable." Id. at 8. Accordingly, the public and the Office understood that discovery was not available in *inter partes* reexamination, and that additional legislation would be required to provide for such discovery.

On September 16, 2011, Congress enacted The America Invents Act (the AIA), which, replaces *inter partes* reexamination with a new proceeding titled *inter partes* review, effective September 16, 2012. The statute expressly provides for discovery in newly enacted 35 U.S.C. § 316 (Conduct of *inter partes* review), which instructs the Director to "prescribe regulations . . . setting forth standards and procedures for discovery of relevant evidence, including that such discovery will be limited to (A) the deposition of witnesses submitting affidavits or declarations; and (B) what is necessary in the interests of justice." See Pub. L. No. 112-29, Section 6. The legislative history of the new proceeding confirms that Congress intended to provide discovery where none had previously been available:

> The Act converts inter partes reexamination from an examinational to an adjudicative proceeding, and renames the proceeding ''inter partes review.'' The Act also makes the following improvements to this proceeding:
>
> . . . .
>
> • Discovery. Parties may depose witnesses submitting affidavits or declarations and seek such discovery as the Patent Office determines is otherwise necessary in the interest of justice.
>
> H. Rep. No. 112-98 (Part 1) 112th Cong., 1st Sess., at 46-47 (2011) (available at http://www.gpo.gov/fdsys/pkg/CRPT-112hrpt98/pdf/CRPT-112hrpt98-pt1.pdf).

Congress's characterization of the provision for limited discovery in *inter partes* review as an "improvement" over *inter partes* reexamination settles any dispute concerning the proper interpretation of the *inter partes* reexamination statute. The AIPA does not authorize discovery in *inter partes* reexamination proceedings.

The patent owner argues that case law relating to discovery in patent interferences supports the ability to obtain discovery under 35 U.S.C. 24 without prior Office approval. However, the enactment of the *inter partes* review discovery provision of the AIA, which sets limits on permissible discovery in *inter partes* review, confirms that the patent owner cannot rely on 35 U.S.C. 24 in isolation to provide authorization for discovery in Office proceedings. The anomalous result of patent owner's argument would be that because the *inter partes* reexamination statute failed to provide for discovery, more discovery would be available under *inter partes* reexamination than under *inter partes* review. That result is plainly contrary to Congress's intent.

Furthermore, 35 U.S.C. 24 applies to contested cases within the Patent and Trademark Office. However, an *inter partes* reexamination proceeding is not a contested case, also as argued by the third party requester of the '552 proceeding.[2] The Office's interpretation of 35 U.S.C. 314 to exclude authorization for discovery in *inter partes* reexamination proceedings, including the interpretation that *inter partes* reexamination proceedings are not "contested cases" within the meaning of 35 U.S.C. 24, is confirmed by the Office's promulgation of rules specifically governing discovery for interferences, while none were drafted for *inter partes* reexamination proceedings. *See, e.g.*, 37 CFR 41.150(a), which states: "[a] party is not entitled to discovery except as authorized in this subpart". Finally, if Congress intended to permit discovery in *inter partes* reexamination proceedings, it would have modeled those proceedings on "contested cases" such as interferences, and not on proceedings such as initial examination or *ex parte* reexamination, which are not contested cases, and which do not include discovery. *See, e.g.*, 145 Cong. Rec. H6944 (Aug. 3, 1999) (Statement of Rep. Rohrabacher) (indicating that the AIPA was intended to create a proceeding like ex parte reexamination which did "not subject the patent to any greater challenge in scope than currently exists today" but "merely allows a reexam requestor the option to further explain why a particular patent should not have been granted").

In summary, discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute, or by any regulation governing *inter partes* reexamination proceedings. 35 U.S.C. 24 is not applicable to *inter partes* reexamination proceedings.

Accordingly, patent owner's October 7, 2011 petition under 37 CFR 1.182 is **denied**. For the same reasons, patent owner's October 7, 2011 alternative petition under 37 CFR 1.182, requesting the Office to authorize discovery under 35 U.S.C. 24 in the present merged proceeding, is also **denied**.

This decision constitutes the Office's final decision concerning whether discovery is permissible in *inter partes* reexamination proceedings.

---

[2] See the November 2, 2011 opposition by the third party requester, Abbott Laboratories, of *inter partes* reexamination proceeding 95/000,552.

CONCLUSION

- Patent owner's October 7, 2011 petition under 37 CFR 1.182 is **denied**.
- Patent owner's October 7, 2011 alternative petition under 37 CFR 1.182, requesting the Office to authorize discovery under 35 U.S.C. 24 in the present merged proceeding, is **denied**.
- This decision is designated as a final agency action under 5 U.S.C. § 704.
- Any inquiry concerning this communication should be directed to Cynthia Nessler, Senior Legal Advisor, at (571) 272-7724.

Brian E. Hanlon
Director
Office of Patent Legal Administration

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/000,542 ~~95000552~~	04/15/2010	7,591,844 B2	CRDS-0116	8264

45511 7590 05/15/2014

Baker & Hostetler LLP
CIRA CENTRE, 12TH FLOOR
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PHILADELPHIA, PA 19104-2891

EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	**PAPER NUMBER**
3991	

MAIL DATE	DELIVERY MODE
05/15/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patents and Trademark Office
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THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS
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745 FIFTH AVENUE
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NEW YORK, NY 10151

Date:

MAILED

MAY 15 2014

CENTRAL REEXAMINATION UNIT

Transmittal of Communication to Third Party Requester
Inter Partes Reexamination

REEXAMINATION CONTROL NO. : 95000542 + 95000552
PATENT NO. : 7591844
ART UNIT : 3993

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the inter partes reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an ex parte reexamination has been merged with the inter partes reexamination, no responsive submission by any ex parte third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the Central Reexamination Unit at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/000,552 + 95000542	06/14/2010	7591844	01035.0068-00000	9463

45511 7590 05/15/2014

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HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
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MAIL DATE	DELIVERY MODE
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UNITED STATES PATENT AND TRADEMARK OFFICE

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MAY 15 2014
CENTRAL REEXAMINATION UNIT

Transmittal of Communication to Third Party Requester
Inter Partes Reexamination

REEXAMINATION CONTROL NO. : 95000552 +95000542
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ART UNIT : 3991

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the inter partes reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an ex parte reexamination has been merged with the inter partes reexamination, no responsive submission by any ex parte third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the Central Reexamination Unit at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

United States Patent and Trademark Office

Commissioner for Patents
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MAILED

MAY 15 2014

CENTRAL REEXAMINATION UNIT

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Washington, D.C. 20001-4413

Inter Partes Reexamination Proceeding
Control No. 95/000,542
Filed: April 15, 2010
For: U.S. Patent No.: 7,591,844

Inter Partes Reexamination Proceeding
Control No. 95/000,552
Filed: June 14, 2010
For: U.S. Patent No. 7,591,844

DECISION DENYING PETITION

This decision addresses the following:

- Patent owner's June 12, 2013 paper entitled "Patent Owner's Supplemental Submission in Support of Petition for Director's Exercise of Statutory Authority" (patent owner's June 12, 2013 petition);

- Requesters' July 9, 2013 joint opposition paper entitled "Requesters Abbott's and Boston Scientific's Opposition to Patent Owner's June 12, 2013 'Supplement Submission' Seeking Discovery in *Inter Partes* Reexamination Proceedings" (requesters' July 9, 2013 joint opposition); and

- Requesters' July 9, 2013 joint petition entitled "Requesters Abbott's and Boston Scientific's Petition to Respond to Patent Owner's June 12, 2013 'Supplement Submission' Seeking Discovery in *Inter Partes* Reexamination Proceedings" (requesters' July 9, 2013 joint petition to enter and consider requesters' joint opposition).

Patent owner's June 12, 2013 petition; requesters' July 9, 2013 joint opposition, requesters' July 9, 2013 joint petition, and the record as a whole, are before the Office of Patent Legal Administration for consideration.

SUMMARY

Patent owner's June 12, 2013 petition is **granted to the extent that** the Office's December 7, 2011 decision has been reconsidered, but is **denied** as to the underlying relief requested.

Requesters' July 9, 2013 joint petition to enter and consider requesters' joint opposition has been **granted to the extent that** requesters' joint opposition has been entered, and has been considered to the extent set forth in this decision.

This decision is designated as a final agency action under 5 U.S.C. § 704.

DECISION

Jurisdiction

The patent owner argues that the issues set forth in its present combined petition must be decided by an individual appointed pursuant to the Appointments Clause of the United States Constitution ("Clause"). The Office takes no position on whether the act of deciding the present combined petition involves the exercise of "sovereign authority" such that the individual rendering the decision must be appointed as an "inferior officer" under the Clause. The question here is moot because the undersigned individual issuing this decision has been appointed by the Secretary of Commerce as a "Petitions Officer" pursuant to the Clause.

Patent Owner's June 12, 2013 Petition

The patent owner requests reconsideration, in view of the Federal Circuit decision in *Abbott Labs. v. Cordis Corp.*, 710 F.3d 1318 (Fed. Cir. 2013), of the Office's December 7, 2011 decision denying patent owner's earlier petition under 37 CFR 1.182, filed on October 7, 2011. Patent owner's earlier petition requested the Office to "confirm that its current rules impose no requirement that parties seeking to enforce subpoenas under [35 U.S.C.] § 24 must obtain the Office's authorization", or alternatively, to "grant such authorization". In denying the petition, the Office determined that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute or by any regulation governing *inter partes* reexamination proceedings, and that *inter partes* reexamination proceedings are not "contested cases" within the meaning of 35 U.S.C. 24.

In *Abbott Labs*, the Federal Circuit held (emphasis in original):

> We conclude that *section 24* only empowers a district court to issue a subpoena for use in a "contested case," and that contested cases are limited to those in which the regulations of the United States Patent and Trademark Office ("PTO") authorize the parties to take depositions. Since the PTO does not provide for

> depositions in inter partes reexamination proceedings, such proceedings are not "contested cases" within the meaning of *section 24*, and subpoenas under *section 24* are not available. We affirm.

710 F.3d at 1319-1320.

The Federal Circuit thus affirmed the Office's "interpretation that *inter partes* reexamination proceedings are not 'contested cases' within the meaning of 35 U.S.C. 24," (December 7, 2011 decision, at 6) and for this reason, subpoenas under 35 U.S.C. 24 are not available in *inter partes* reexamination proceedings.

The patent owner alleges that "the PTO was previously operating under an incorrect understanding of the Patent Act", and that the Office's position that discovery is not permitted by the *inter partes* reexamination statute is inconsistent with the Federal Circuit's holding in *Abbott Labs.* The patent owner apparently alleges that the court held that "the [*inter partes* reexamination] statute does not preclude the issuance of subpoenas in *inter partes* reexaminations."

The patent owner, however, mischaracterizes the Federal Circuit's decision. There is nothing in the Federal Circuit's decision that suggests that the Office misinterpreted the *inter partes* reexamination statute. The Federal Circuit determined:

1. 35 U.S.C. 24 only empowers a district court to issue a subpoena for use in a "contested case."
2. Contested cases are limited to those proceedings in which the regulations of the Office provide for the taking of depositions for use in that proceeding.
3. There are no Office regulations that permit the taking of depositions in *inter partes* reexamination proceedings.
4. *Inter partes* reexamination proceedings are not contested cases within the meaning of 35 U.S.C. 24 because there are no Office regulations authorizing the parties to take depositions in such proceedings.
5. Subpoenas under 35 U.S.C. 24 are not available in *inter partes* reexamination proceedings.

The decision in *Abbott Labs* is silent as to whether the Office is authorized under the *inter partes* reexamination statute to permit discovery in *inter partes* reexamination proceedings. Because there are no Office regulations permitting the taking of depositions in *inter partes* reexamination proceedings, and, for this reason, subpoenas under 35 U.S.C. 24 are not available in *inter partes* reexamination proceedings, the Federal Circuit had no need to address whether such regulations would be authorized specifically by the *inter partes* reexamination statute. The Federal Circuit did not reach the issue of whether the *inter partes* reexamination statute authorized the Office to permit discovery in such proceedings, also as pointed out by the requesters in their joint opposition. Thus, contrary to patent owner's arguments, the December 7, 2011 decision, which determined that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute, is not inconsistent with the Federal Circuit's holding in *Abbott Labs.*

For these reasons, the patent owner's June 12, 2013 petition is **granted** to the extent that the Office's December 7, 2011 decision has been reconsidered, but is **denied** with respect to making any changes therein.

The patent owner also requests the Office to exercise its "particularized rulemaking authority" to permit discovery in this case and impose a duty of candor on the third party requesters. The Office has wide discretion to choose between rulemaking and adjudication for adopting procedural rules. *SEC v. Chenery*, 332 U.S. 194, 203 (1947) ("[T]he choice made between proceeding by general rule or by individual, *ad hoc* litigation is one that lies primarily in the informed discretion of the administrative agency"). It has been the Office's position that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute. Therefore, the Office has not promulgated the regulations requested. Even if, arguendo, the Office has that authority, the Office does not believe that rules regarding discovery and the duty of candor in *inter partes* reexaminations should be adopted through case-by-case adjudication, for at least the following reasons: (1) in case-by-case adjudication, the Office will only have the input of two parties; and (2) the Office believes, based on its experience and expertise, that it is impractical and unfair to participants to set rules for *inter partes* reexamination proceedings on an *ad hoc* basis. Accordingly, the Office will not, at this time, in the context of this adjudication, exercise any authority, should the Office have it, to promulgate a regulation or regulations permitting discovery and imposing a duty of candor on third party requesters in *inter partes* reexamination proceedings.

Accordingly, patent owner's June 12, 2013 petition is **granted to the extent that** the Office's December 7, 2011 decision has been reconsidered, but is **denied** as to the underlying relief requested.

If the patent owner later wishes to petition the Office under 5 U.S.C. 553(e) to exercise its rulemaking authority and, for example, promulgate regulations governing all *inter partes* reexamination proceedings, the patent owner must file a petition under separate cover, directed to the Deputy Under Secretary of Commerce for Intellectual Property and Deputy Director of the United States Patent and Trademark Office. Such a petition must not be filed in a particular application or proceeding, and must not be directed to a particular application or proceeding.

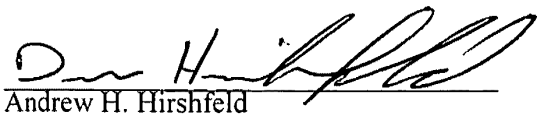
CONCLUSION

- Patent owner's June 12, 2013 petition is **granted to the extent that** the Office's December 7, 2011 decision has been reconsidered, but is **denied** as to the underlying relief requested.

- Requesters' July 9, 2013 joint petition to enter and consider requesters' joint opposition has been **granted to the extent that** requesters' joint opposition has been entered, and has been considered to the extent set forth in this decision.

- This decision is designated as a final agency action under 5 U.S.C. § 704.

- Any inquiry concerning this communication should be directed to Cynthia Nessler, Senior Legal Advisor, at (571) 272-7724.



Andrew H. Hirshfeld
Deputy Commissioner for Patent Examination Policy
Petitions Officer
United States Patent and Trademark Office
Department of Commerce

May 1, 2014

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/000,542 + 95/000,552	04/15/2010	7,591,844 B2	CRDS-0116	8264

45511 7590 12/04/2014

Baker & Hostetler LLP
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PHILADELPHIA, PA 19104-2891

EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
12/04/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patents and Trademark Office
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Date:

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DEC 04 2014
CENTRAL REEXAMINATION UNIT

Transmittal of Communication to Third Party Requester
Inter Partes Reexamination

REEXAMINATION CONTROL NO. : 95000542 + 95000552
PATENT NO. : 7591844
ART UNIT : 3993

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the inter partes reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an ex parte reexamination has been merged with the inter partes reexamination, no responsive submission by any ex parte third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the Central Reexamination Unit at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

UNITED STATES PATENT AND TRADEMARK OFFICE

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901 NEW YORK AVENUE N.W.
WASHINGTON, DC 2001-4413

Date:

MAILED
DEC 04 2014
CENTRAL REEXAMINATION UNIT

Transmittal of Communication to Third Party Requester
Inter Partes Reexamination

REEXAMINATION CONTROL NO. : 95000552 & 95000542
PATENT NO. : 7591844
ART UNIT : 3991

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If an ex parte reexamination has been merged with the inter partes reexamination, no responsive submission by any ex parte third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the Central Reexamination Unit at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

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(For *Inter Partes* '552 Requester)

Inter Partes Reexamination Proceeding
Control No. 95/000,542
Filed: April 15, 2010
For: U.S. Patent No.: 7,591,844

Inter Partes Reexamination Proceeding
Control No. 95/000,552
Filed: June 14, 2010
For: U.S. Patent No. 7,591,844

DECISION DENYING PETITION

This decision addresses the following:

- Patent owner's June 12, 2013 paper entitled "Patent Owner's Supplemental Submission in Support of Petition for Director's Exercise of Statutory Authority" (patent owner's June 12, 2013 petition);

- Requesters' July 9, 2013 joint opposition paper entitled "Requesters Abbott's and Boston Scientific's Opposition to Patent Owner's June 12, 2013 'Supplemental Submission' Seeking Discovery in *Inter Partes* Reexamination Proceedings" (requesters' July 9, 2013 joint opposition); and

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Patent owner's June 12, 2013 petition; requesters' July 9, 2013 joint opposition, requesters' July 9, 2013 joint petition, and the record as a whole, are before the Commissioner for Patents for consideration.

SUMMARY

Patent owner's June 12, 2013 petition is **granted to the extent that** the Office's December 7, 2011 decision has been reconsidered, but is **denied** as to the underlying relief requested.

Requesters' July 9, 2013 joint petition to enter and consider requesters' joint opposition has been **granted to the extent that** requesters' joint opposition has been entered, and has been considered to the extent set forth in this decision.

DECISION

Jurisdiction

The patent owner argues that the issues set forth in its present combined petition must be decided by an individual appointed pursuant to the Appointments Clause of the United States Constitution. The Office takes no position on whether the act of deciding the present combined petition involves the exercise of "sovereign authority" such that the individual rendering the decision must be appointed as an "inferior officer" under the Appointments Clause. The question here is moot because the undersigned individual issuing this decision has been properly appointed pursuant to the Appointments Clause.

Patent Owner's June 12, 2013 Petition

The patent owner requests reconsideration, in view of the Federal Circuit decision in *Abbott Labs. v. Cordis Corp.*, 710 F.3d 1318 (Fed. Cir. 2013), of the Office's December 7, 2011 decision denying patent owner's earlier petition under 37 CFR 1.182, filed on October 7, 2011. Patent owner's earlier petition requested the Office to "confirm that its current rules impose no requirement that parties seeking to enforce subpoenas under [35 U.S.C.] § 24 must obtain the Office's authorization", or alternatively, to "grant such authorization". In denying the petition, the Office determined that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute or by any regulation governing *inter partes* reexamination proceedings, and that *inter partes* reexamination proceedings are not "contested cases" within the meaning of 35 U.S.C. 24.

In *Abbott Labs*, the Federal Circuit held (emphasis in original):

> We conclude that *section 24* only empowers a district court to issue a subpoena for use in a "contested case," and that contested cases are limited to those in which the regulations of the United States Patent and Trademark Office ("PTO") authorize the parties to take depositions. Since the PTO does not provide for depositions in inter partes reexamination proceedings, such proceedings are not

> "contested cases" within the meaning of *section 24*, and subpoenas under *section 24* are not available. We affirm.

710 F.3d at 1319-1320.

The Federal Circuit thus affirmed the Office's "interpretation that *inter partes* reexamination proceedings are not 'contested cases' within the meaning of 35 U.S.C. 24," (December 7, 2011 decision, at 6) and for this reason, subpoenas under 35 U.S.C. 24 are not available in *inter partes* reexamination proceedings.

The patent owner alleges that "the PTO was previously operating under an incorrect understanding of the Patent Act", and that the Office's position that discovery is not permitted by the *inter partes* reexamination statute is inconsistent with the Federal Circuit's holding in *Abbott Labs.* The patent owner apparently alleges that the court held that "the [*inter partes* reexamination] statute does not preclude the issuance of subpoenas in *inter partes* reexaminations."

The patent owner, however, mischaracterizes the Federal Circuit's decision. There is nothing in the Federal Circuit's decision that suggests that the Office misinterpreted the *inter partes* reexamination statute. The Federal Circuit determined:

1. 35 U.S.C. 24 only empowers a district court to issue a subpoena for use in a "contested case."
2. Contested cases are limited to those proceedings in which the regulations of the Office provide for the taking of depositions for use in that proceeding.
3. There are no Office regulations that permit the taking of depositions in *inter partes* reexamination proceedings.
4. *Inter partes* reexamination proceedings are not contested cases within the meaning of 35 U.S.C. 24 because there are no Office regulations authorizing the parties to take depositions in such proceedings.
5. Subpoenas under 35 U.S.C. 24 are not available in *inter partes* reexamination proceedings.

The decision in *Abbott Labs* is silent as to whether the Office is authorized under the *inter partes* reexamination statute to permit discovery in *inter partes* reexamination proceedings. Because there are no Office regulations permitting the taking of depositions in *inter partes* reexamination proceedings, and, for this reason, subpoenas under 35 U.S.C. 24 are not available in *inter partes* reexamination proceedings, the Federal Circuit had no need to address whether such regulations would be authorized specifically by the *inter partes* reexamination statute. The Federal Circuit did not reach the issue of whether the *inter partes* reexamination statute authorized the Office to permit discovery in such proceedings, also as pointed out by the requesters in their joint opposition. Thus, contrary to patent owner's arguments, the December 7, 2011 decision, which determined that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute, is not inconsistent with the Federal Circuit's holding in *Abbott Labs.*

For these reasons, the patent owner's June 12, 2013 petition is granted to the extent that the Office's December 7, 2011 decision has been reconsidered, but is denied with respect to making any changes therein.

The patent owner also requests, in its June 12, 2013 petition, that the Office exercise its "particularized rulemaking authority" to permit discovery in this case and impose a duty of candor on the third party requesters. The Office has wide discretion to choose between rulemaking and adjudication for adopting procedural rules. *SEC v. Chenery*, 332 U.S. 194, 203 (1947) ("[T]he choice made between proceeding by general rule or by individual, *ad hoc* litigation is one that lies primarily in the informed discretion of the administrative agency"). It has been the Office's position that discovery in an *inter partes* reexamination proceeding is not permitted by the *inter partes* reexamination statute. Therefore, the Office has not promulgated the regulations requested. Even if, arguendo, the Office has that authority, the Office does not believe that rules regarding discovery and the duty of candor in *inter partes* reexaminations should be adopted through case-by-case adjudication, for at least the following reasons: (1) in case-by-case adjudication, the Office will only have the input of two parties; and (2) the Office believes, based on its experience and expertise, that it is impractical and unfair to participants to set rules for *inter partes* reexamination proceedings on an *ad hoc* basis. Accordingly, the Office will not, at this time, in the context of this adjudication, exercise any authority, should the Office have it, to promulgate a regulation or regulations permitting discovery and imposing a duty of candor on third party requesters in *inter partes* reexamination proceedings.

Accordingly, patent owner's June 12, 2013 petition is **granted to the extent that** the Office's December 7, 2011 decision has been reconsidered, but is **denied** as to the underlying relief requested.

CONCLUSION

- Patent owner's June 12, 2013 petition is **granted to the extent that** the Office's December 7, 2011 decision has been reconsidered, but is **denied** as to the underlying relief requested.

- Requesters' July 9, 2013 joint petition to enter and consider requesters' joint opposition has been **granted to the extent that** requesters' joint opposition has been entered, and has been considered to the extent set forth in this decision.

- This decision constitutes the Office's final decision on these issues.

- Any inquiry concerning this communication should be directed to Cynthia Nessler, Senior Legal Advisor, at (571) 272-7724.

Margaret A. Focarino
Commissioner for Patents
United States Patent and Trademark Office
Department of Commerce

December 4, 2014

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/000,542	04/15/2010	7,591,844 B2	CRDS-0116	8264

45511 7590 02/27/2015

Baker & Hostetler LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
02/27/2015	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

UNITED STATES PATENT AND TRADEMARK OFFICE

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95/000,552	06/14/2010	7591844	01035.0068-00000	9463

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PTOL-90A (Rev. 04/07)

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BOSTON SCIENTIFIC SCIMED and ABBOTT LABORATORIES
Requester and Respondent

v.

Patent of
CORDIS CORP., A JOHNSON & JOHNSON CO., and WYETH, A PFIZER CO.
Patent Owner and Appellant

Appeal 2014-008135
Reexamination Control 95/000,542 and 95/000,552
Patent 7,591,844 B2
Technology Center 3900

Before ROMULO H. DELMENDO, RICHARD M. LEBOVITZ, and JEFFREY B. ROBERTSON, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on the appeal by Patent Owner from the Patent Examiner's final rejection of claims 1–17 and 19–23 as obvious under 35 U.S.C. § 103 in the above-identified merged *inter partes* reexaminations of United States Patent

7,591,844 B2. The Board's jurisdiction for this appeal is under 35 U.S.C. §§ 6(b), 134, and 315 (pre-AIA). We affirm.

BACKGROUND

The patent in dispute in this appeal is US 7,591,844 B2 ("the '844 patent") which issued September 22, 2009. The real parties in interest and assignees are Cordis Corporation, a Johnson & Johnson company, and Wyeth, a Pfizer company ("Patent Owner"). Appeal Br. 1 (October 17, 2012). Patent Owner appeals the Examiner's final rejection of claims 1–17 and 19–23.

A request for *inter partes* reexamination of the '844 patent was filed April 15, 2010 by Boston Scientific SCIMED, Inc. under 35 U.S.C. §§ 311–318 and 37 C.F.R. §§ 1.902–1.997. A second request for *inter partes* reexamination was filed June 14, 2010 by Abbott Laboratories. The reexaminations were merged into a single proceeding. Decision, *Sua Sponte* Merging *inter partes* proceedings (Nov. 26, 2010).

An oral hearing was held January 21, 2015. A transcript of the hearing has been entered into the record ("Hearing Tr.").

The claimed subject matter of the '844 patent relates to a device for intraluminal implantation in a vessel comprising a "balloon expandable stent" and a "pharmaceutical agent-containing coating." The coating comprises vinylidinefluoride (VDF) copolymerized with hexafluoropropylene (HFP) in a weight percent ratio of 85:15. According to the '844 patent, transluminal angioplasty can be used to increase blood flow through a blocked artery by widening the artery through the use of an expandable balloon stent. '844, cols. 1–2. Although angioplasty has a short-term immediate benefit, the benefit is not always

lasting."Upon pressure expansion of an intracoronary balloon catheter during angioplasty, smooth muscle cells within the vessel wall become injured, initiating a thrombotic and inflammatory response." *Id.* at col. 2, ll. 10–13. As a result, the vascular wall can narrow again in a process called "restenosis." *Id.* at col. 1, ll. 46–51; col. 2, ll. 33–35. The '844 patent teaches that stent coatings containing a pharmaceutical agents may be used to reduced restenosis. *Id.* at col. 4, ll. 43–54. The patent teaches in the "Background of the Invention" that "[s]tents with coatings made from polyvinylidenefluoride [VDF] homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested." '844 patent, col. 5, ll. 4–6.

CLAIM 1

Independent claims 1 and 19 are the only independent claims involved in the appeal. Claim 1 is drawn to a device and claim 19 to a method of preparing a device. Claim 1 is representative and reads as follows (abbreviations within braces added):

> 1. A device for intraluminal implantation in a vessel comprising a balloon-expandable stent and a pharmaceutical agent-containing coating, said coating comprising a biocompatible polyfluoro copolymer that comprises about eighty-five weight percent vinylidinefluoride {VDF} copolymerized with about fifteen weight percent hexafluoropropylene {HFP} and at least one pharmaceutical agent intermixed with said copolymer, wherein said coating has not been subjected to a maximum temperature greater than 60° C during the coating process or afterward, thereby providing an adherent coating that remains adhered to the device upon expansion of the balloon-expandable stent.

REJECTIONS

The claims stand rejected by the Examiner over 33 different combinations of publications. Appeal Br. 4–6; Abbott Respondent Br. 1. Each of the rejections of independent claims 1 and 19 is based on substantially the same factual underpinnings, but relies on different publications for the same set of facts. Rather than addressing each ground separately, Patent Owner has focused its arguments on the factual basis of the rejections, grouping their arguments together for the various grounds of rejection of the independent claims. The rejections of the dependent claims were not argued separately.

For clarity, the table below summarizes the ten different grounds of rejection which involve independent claims 1 and 19. The rejections which involve dependent claims only have not been listed since they were not separately argued. There are three main groups of publications: 1) Tuch,[1] Wright, Kamath, and Patent Owner's Admissions, each of which is cited for teaching a stent coated with a polymer comprising a therapeutic agent: 2) Tu[2] and Lilenfeld, each of which is cited for teaching of a medical device comprising VDF:HFP; and 3) Lo[3], Wille, and Modern Fluoropolymer, each of which is cited for teaching of VDF:HFP in the claimed wt% of 85:15.

[1] Tuch	US 5,824,048	Oct. 20, 1998
[2] Tu et al. (Tu)	US 4,816,339	Mar. 28, 1989
[3] Lo	US 3,178,399	Apr. 13, 1965

	1	2	3	4	5	6	7	8	9	10
	1-17, 19-23	1-15,19-21	1-15, 19-21	1-15, 19-21	1-15,19-21	1-17, 19-23	1-17,19-23	1,2,8,19,20	1,2,8,19,20	1,2,8,19,20
Tuch		Y	Y	Y	Y					
Wright						Y	Y			
Kamath								Y	Y	Y
Pat. Admission	Y									
Tu	Y	Y		Y	Y	Y	Y	Y	Y	Y
Lilenfeld			Y							
Lo	Y	Y				Y		Y		
Wille				Y			Y		Y	
Modern Fluoropolymers					Y					Y

The table above shows the ten different grounds over the independent claims. Because the rejections were argued together, we have focused on the rejection based on Tuch, Tu, and Lo (rejection 2, above), and have not reached rejections 1 and 3–10, although as recognized by Patent Owner, similar rationale would apply.

In addition to the prior art publications, the following declarations have been cited as evidence:

First Declaration by Antonios G. Mikos, Ph.D ("First Mikos Decl.") dated Aug. 27, 2010. Dr. Mikos was a Professor of Bioengineering and Chemical and Biomolecular Engineering in the Departments of Bioengineering and Chemical and Biomolecular Engineering at Rice University at the time the declaration was executed. First Mikos Decl. ¶ 1. Dr. Mikos testified that he has expertise in the synthesis, fabrication and application of biomaterials, specifically polymers, for medical applications, including cardiovascular applications. *Id.* at ¶ 3. Dr. Mikos testified on behalf of the Patent Owner.

2012 Declaration by Michael N. Helmus, Ph.D. ("2012 Helmus Decl.") dated March 30, 2012. Dr. Helmus testified that he is an expert in biomaterials, biocompatibility, and biomaterial databases for medical device applications and currently works as a consult in the field of medical devices. Dr. Helmus testified on behalf of Abbott.

SCOPE AND CONTENT OF THE PRIOR ART[4]

Tuch

Tuch1. Tuch describes an intravascular stent that has a coating on its tissue-contacting surface which comprises a polymer and therapeutic substance. Tuch, col. 2, ll. 36–38.

Tuch2. Tuch teaches that the stent can be of any design, including self-expanding and balloon-expandable types. *Id.* at col. 4, ll. 10–13.

Tuch3. Tuch discloses that the polymer must be biocompatible and minimize irritation to the vessel wall when the stent is implanted. *Id.* at col. 5, ll. 14–16.

Tuch4. Tuch also teaches that the polymer may be either biostable or bioabsorbable. *Id.* at col. 5, ll. 15–16.

Tuch5. Tuch describes "biostable polymers with a relatively low chronic tissue response." *Id.* at col. 5, ll. 33–34.

Tuch6. The list of the biostable polymers includes "vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride [VDF] and polyvinylidene chloride." *Id.* at col. 5, ll. 38–42.

Tuch7. Tuch teaches that during implantation of an expandable stent, the delivery balloon expands and deforms the stent elements and coating. *Id.* at col. 7, ll. 9–11.

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[4] Factual considerations that underlie the obviousness inquiry include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

Tuch8. When the polymeric overlayer on the stent is uniform and "made with materials which have little elasticity," Tuch teaches that "the overlayer can sustain significant cracking during such deformation" and the "cracks can then act as channels for more rapid elution of drugs from the drug-rich base coating." *Id.* at col. 7, ll. 11–15.

Tuch9. Tuch teaches that "cracking of the overlayer can be reduced and drug elution times increased by providing a porous overlayer on the stent." *Id.* at col. 7, ll. 16–18.

Tuch10. Tuch teaches that the coating should be "resilient"[5] for stent expansion: "The inclusion of a polymer in intimate contact with a drug on the stent allows the drug to be retained on the stent in a resilient matrix during expansion of the stent . . ." *Id.* at 2:42–46. In context, Tuch uses the term "resilient" to have its ordinary meaning, which is to be "able to return to an original shape after being pulled, stretched, pressed, bent, etc.," a synonym being "elastic."

Tu

Tu1. Tu describes implantable biomedical devices formed with layers of polytetrafluoroethylene, polytetrafluoroethylene/elastomer, and elastomer. Tu, col 2, ll. 7–37.

Tu2. Tu teaches that its invention relates to various types of implantable bioomedical devices, including heart valve leaflets, and the invention particularly relates to vascular grafts. *Id.* at col. 1, ll. 27–32; col. 2, ll. 36–40.

[5] "Resilient" means "able to return to an original shape after being pulled, stretched, pressed, bent, etc." and a synonym is "elastic." http://www.merriam-webster.com/dictionary/resilient (accessed Jan. 28, 2015).

Tu3. Tu discloses a list of compounds used to prepare the elastomer. *Id.* at col. 2, ll. 20–30. Polyvinylidene fluoride co-hexafluoropropylene (VDF:HFP) is first on the list. *Id.* at col. 2, ll. 23–24.

Tu4. Tu teaches that the elastomer provides elasticity and strength. *Id.* at col. 3, ll. 40–44, 64.

Tu5. According to Tu, the "elastomer solution may optionally contain therapeutic agents including but not limited to antibiotic and/or hemostatic substances." *Id.* at col. 8, ll. 45–47.

Tu6. Tu teaches that the implantable material made of polytetrafluoroethylene and elastomer is biologically compatible. Id. at col. 2, ll. 11–19, 31; col. 3, l.

Lo

Lo1. Lo describes copolymers of vinylidene fluoride (VDF) and hexafluoropropene (HFP) which have flexibility, elasticity, and extensibility. Lo, col. 2, ll. 33–36, 47, and 56–58.

Lo2. Figure 1 of Lo shows an increase of tensile PSIG and reversible elongation from about 86 mol percent to a maximum of about 94 mol percent with a copolymer made of vinylidene fluoride and hexafluropropene.

Lo3. Lo teaches that "[a]bove about 94 mol percent vinylidene fluoride (i.e. less than 6 mol percent hexafluoropropene) the copolymer is essentially crystalline in nature and the reversible elongation decreases rapidly." Lo, col. 9, ll. 33–36.

Lo4. The Examiner found that "copolymers with an optimal combination of tensile strength and reverse elongation are achieved at 93 mol % VDF, corresponding to a VDF/HFP wt% ratio of 85:15 (Fig. 1; col. 9, lines 15–27)."

RAN 14. Dr. Mikos in his declaration acknowledged that "Lo describes VDF/HFP coatings having VDF:HFP weight percent of 85: 15." First Mikos Decl. ¶ 41.

Le Morel[6]

LeM1. LeMorel teaches implants such as stents. LeMorel 2:4–15.

LeM2. Le Morel teaches that the substrate of the implant can be a polymer, and specifically identifies copolymers of vinylidene fluoride and hexafluorpropylene among a list. *Id.* at 3:1–5 and 18–19.

LeM3. Le Morel teaches in the case of stents, a fluorinated polymer is advantageous. *Id.* at 4:4–10.

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE PRIOR ART

The Examiner found that Tuch describes a balloon-expandable stent having a coating containing a therapeutic agent, meeting the claimed limitation of "a balloon-expandable stent and a pharmaceutical agent-containing coating." RAN 13-14; Tuch1–2, 7. The Examiner found that the coating may be formed with VDF. RAN 14; Tuch6. The Examiner found that Tuch does not describe a coating "that comprises about eighty-five weight percent vinylidinefluoride [VDF] copolymerized with about fifteen weight percent hexafluoropropylene [HFP]," but found that Lo describes such a copolymer coating and its advantages with respect tensile strength and reversible elongation. RAN 14; Lo1–4. Furthermore, the

[6] Le Morel et al. (Le Morel or LeM) FR 2,785,812 Nov. 16, 1998. Citations to translation of record.

Examiner found that Tu demonstrates the biocompatibility of VDF/HFP polymers and that such copolymers can contain therapeutic substances. RAN 14; Tu5.

Based on the teachings of Lo and Tu, the Examiner determined it would have been obvious to one of ordinary skill in the art to have replaced "Tuch's crystalline VDF homopolymer with the partially crystalline copolymers having a VDF/HFP wt % ratio of about 85:15 (as recited in [device] claim 1 and method claim 19) . . . to arrive [at] the instant invention." RAN 14–15. The Examiner's rationale was that a person of ordinary skill in the art would have understood that VDF/HFP is advantageous as compared to VDF homopolymers and has optimal tensile strength and reversible elongation at VDF/HFP wt% ratio of 85:15 as shown by Lo. *Id.* at 14.

Discussion

Patent Owner contends that the Examiner erred in combining the publications to have arrived at the claimed invention. Specifically, Patent Owner argues that one of ordinary skill in the art reading Tuch would not have had reason to choose polymers from publications other than Tuch because Tuch did not identify a problem with its polymers used for its drug coating layer. Appeal Br. 16. Patent Owner also argues that it is improper to combine Tu's teachings with those of Tuch. *Id.* at 17.

Choice of VDF:HFP

It is unnecessary that Tuch disclose any shortcomings in its list of polymers for the ordinary skilled worker to have found it obvious to have employed an alternative polymer for its coating since it is obvious to use a prior art element for

its established function. As held in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007), in making an obviousness determination, it must be asked "whether the improvement is more than the predictable use of prior art elements according to their established functions." Thus, even if Tuch did not disclose a problem with its polymers, one of ordinary skill in the art would have found it obvious to have employed the known polymers of Tu and Lo for their known and expected properties. As argued by Abbott, Abbott Respondent Br. 12, the reason to combine could be provided by the "normal desire of scientists or artisans to improve upon what is already generally known." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003).

In addition to this, Tuch does not limit its polymers to those specifically disclosed. Tuch teaches using "vinyl halide polymers and copolymers," and specifically discloses "polyvinylidene halides, such as polyvinylidene fluoride." Tuch6. This disclosure, while mentioning a specific polyvinylidene halide, also includes broader classes ("vinyl halides" and "polyvinylidene halides"), including copolymers, which would have reasonably suggested that additional polymers, outside those specifically described in Tuch, would be useful as Tuch's polymer coating comprising a therapeutic substance.

To support their position about the unobviousness of using polymers other than those disclosed in Tuch, Patent Owner cites *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342,1370–71 (Fed. Cir. 2012).

> As in *Kinetic Concepts, Inc.* 688 F.3d at 1369, a case in which the Federal Circuit overturned a prior finding of obviousness, the record here "is devoid of any reason someone would combine [the cited] references." Where, as here, each device that the references describe "independently operates effectively," a person having ordinary skill in

> the art "would have no reason" to combine the reference'' respective teachings. *Id.*

Appeal Br. 17. *See* also Rebuttal Br. 3.

In *Kinetic*, the issue was whether to combine publications which "both . . . independently accomplish similar functions, namely, draining fluids." *Kinetic Concepts, Inc.* 688 F.3d at 1369. One set of publications involved negative pressure to drain wounds. *Id.* at 1362-1363. The other set of publications disclosed a different type of wound drainage system. *Id.* at 1365. The obviousness rejection was predicated on combining the two sets of publications to meet a limitation in the claim of using negative pressure to treat a wound, where wound treatment had not been found to be present in the negative pressure publications. *Id.* at 1361, 1363. Because each publication was complete in teaching a wound drainage method, and there was no teaching that negative pressure could be used to treat wounds, the court found "a person having ordinary skill in the art, who was merely seeking to create a better device to drain fluids from a wound, would have no reason to combine the features of both devices into a single device." *Id.* at 1369.

The facts of this case are clearly distinguishable. Tuch teaches various polymer coatings for its stent, including broad classes that encompass unnamed species. Tu was cited in the rejection for teaching polymers suitable for Tuch's stent coating. The reason to consult Tu is because Tuch's list of polymers is clearly not exhaustive in view of Tuch's description of broad classes of polymers, such as vinyl halide polymers and copolymers, and polyvinylidene halides. Tuch6. Tuch also uses the transitional phrase "such as" in prefacing the list of biostable polymers and in reciting specific examples of the broader classes, indicating that Tuch did not confine the skilled worker to the explicit list, but contemplated

polymers outside of it. ("Also, biostable polymers with a relatively low chronic tissue response such as . . . and other polymers could also be used if they can be dissolved and cured or polymerized on the stent such as . . . vinyl halide polymers and copolymers, such as . . . " Tuch, col. 5, ll. 33–39).

Patent Owner argues that Tuch recites a long laundry list of polymers and therefore would not have directed the skilled worker to the specifically claimed polymers. Appeal Br. 24. First Mikos Decl. ¶¶ 52–56.

The fact that "vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride [VDF] and polyvinylidene chloride" appear in a longer list (Tuch6) would not have dissuaded one of ordinary skill from choosing VDF copolymers. The list recited in Tuch is of polymers that Tuch considered useful for its stent coating and therefore is a disclosure of each and every one for a stent coating. There does not have to be a working example of vinyl halide polymer copolymer, polyvinylidene halide, or VDF, as alleged by Dr. Mikos (First Mikos Decl. ¶ 143) for one of ordinary skill in the art to have recognized such compounds as useful for a polymer coating since Tuch expressly describes their use for this purpose. Tuch6.

Furthermore, Patent Owner admitted in the "Background" of the '844 patent that "[s]tents with coatings made from polyvinylidenefluoride homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested." '844 patent, col. 5, ll. 4–6. *See* also "Preexamination Search Statement and Accelerated Examination Support Document" 12 ("AESD"; filed Nov. 16, 2007 in the application that led to the '844 patent) identifying the latter statement as prior art.

Dr. Mikos attempts to distinguish Tuch because Tuch describe a porous overlayer of polymer to control drug release. First Mikos Decl. ¶ 144. However, the claim does not exclude such a porous layer made of VDF:HFP.

Patent Owner also argues that the stent coating in Tuch is in contact with the vessel wall lining and in contact with blood, while in Tu, the graft's inner surface which contacts the blood lacks the elastomer. Appeal Br. 23. While this might be the case, Tu teaches that it's the polytetrafluoroethylene/elastomer which can be used generally in other medical devices, such as a heart valve leaflet that could be in contact with blood. Tu2.

Is there an adequate reason to have combined Tuch and Tu?

Patent Owner argues that the record is devoid of reason to have combined Tuch and Tu. Appeal Br. 17. Patent Owner also argues that Tu relates to vascular grafts and therefore is not relevant to Tuch.[7] *Id.* at 18:1–2.

A preponderance of the evidence does not support Patent Owner's position that the record lacks a reason to combine Tuch with Tu.

First, Tu is not limited to vascular grafts, but clearly teaches that its polymers are useful for various types of implantable devices. Tu2. While vascular grafts are preferred, such preference does not negate the broader teaching.

Second, Tu's polyvinylidene fluoride co-hexafluoropropylene has the properties described in Tuch as useful for its stent coating. These properties are discussed below:

1) Tuch's polymers are biocompatible as they are in Tu. Tuch3; Tu6.

[7] Taking a contrary position, in the AESD filed in the application that led to the '844 patent, Patent Owner characterized Tu (US 5,061,276) as one of the "most closely related" prior art references. AESD 6. Abbott Respondent Br. 15.

2) Tuch teaches elastic polymers are beneficial for coatings in expandable stents. Tuch8, 10. Tu's elastomers are elastic. Tu4.

Patent Owner contends that elasticity would not have been a factor in choosing a polymer coating for Tuch's stent. Appeal Br. 18–19. However, Tuch teaches that, when the stent delivery balloon expands, the stent coating can deform. Tuch7. When materials are used for the polymers which "have little elasticity," the polymer overlayer can crack during the expansion and result in rapid drug elution. Tuch8. Tuch teaches one way to reduce the cracking. Tuch9. Since Tuch teaches a problem with cracking when materials having little elasticity are utilized in the polymer layer, one of ordinary skill in the art would have reasonably sought materials with high elasticity to avoid the problem when the stent is expanded.

Furthermore, Tuch teaches that using a resilient matrix during expansion of the stent is beneficial for drug retention. Tuch10. Resilient is a synonym for elastic. Fn. 5. *See* also 2012 Helmus Decl. ¶ 6 for further evidence of the desirability of an elastic polymer. Tu teaches elastomers that provide elasticity and strength. Tu4.

Dr. Mikos testified that the "physical and mechanical properties that are important for the Tu vascular grafts . . . are very different from the physical and mechanical properties that are important for polymer coatings used on balloon expandable stents [as in Tuch]." First Mikos Decl. ¶ 43. Dr. Mikos identifies elasticity as important in vascular grafts. *Id.* at ¶ 44. Dr. Mikos, however, did not explain how elasticity is distinguishable from the ability of a polymer to be elongated or deformed before breaking which he identified as an "important property" of a stent polymer coating. *Id.* at ¶¶ 46, 147. That is, while Tu's graft may have a different purpose than Tuch's stent, Dr. Mikos admits that a stent

coating must be resilient (resist deformation before breaking) which is the same property that Dr, Mikos identifies as important in vascular grafts. Consequently, Dr. Mikos's testimony about the lack of reason to combine Tuch and Tu is not supported by persuasive factual evidence.

3) Tuch teaches that polyvinylidene fluoride is a useful polymer for its coating comprising a therapeutic substance. Tuch1, 6. The first elastomer on Tu's list is a copolymer comprising polyvinylidene fluoride and hexafluoropropylene (VDF:HFP). Tu3. The obviousness of choosing VDF:HFP as a stent coating is further evidenced by Le Morel who describes the copolymer as coating on a stent. LeM1–3.

4) Tuch teaches a polymer coating that delivers a therapeutic substance. Tuch1. Tu also teaches that its elastomer can contain therapeutic agents. Tu5.

Summary

In sum, a preponderance of the evidence supports the determination it would have been obvious to have selected VDF:HFP from Tu as the polymer coating in Tuch. Contrary to Patent Owner's statement that it would have been a scavenger hunt to find VDF:HFP (Hearing Tr. 4:6–11), VDF:HFP is disclosed by Tu as a useful elastomer for an implantable medical device and Tu's elastomers have the properties described by Tuch as advantageous in a stent, which is an example of an implantable device.

Proportion of VDF and HFP

As far as the 85:15 copolymer of VDF and HFP recited in the claims, Lo teaches that a 85:15 copolymer is advantageous with respect to flexibility,

elasticity, extensibility, tensile strength, and reverse elongation. Lo1–4; RAN 14. One of ordinary skill in the art would have been motivated to have used Lo's polymer having these advantageous properties as the coating in Tuch because Tuch teaches a problem with coatings with low elasticity (Tuch8-9).

Because VDF:HFP is expressly described by Tu as useful for an implantable medical device (Tu2), the skilled worker would have reasonably consulted Lo to determine the optimal concentrations for each component, even if Lo does not teach the use of VDF:HFP for medical implants. Patent Owner's argument that Lo's uses are industrial and therefore not pertinent to stents (Appeal Br. 24; First Mikos Decl. ¶¶ 41–42) is unavailing since Lo was cited for teaching the properties of VDF:HFP which had been taught to be useful by Tu in a medical device.

Patent Owner's argument that VDF:HFP is not described as a carrier for a drug has little merit. Appeal Br. 25. As mentioned, Tu teaches that its elastomer may contain therapeutic agents. Tu5.

SECONDARY CONSIDERATIONS

Factual considerations that underlie the obviousness inquiry include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations. *Graham.*, 383 U.S. at 17-18. Relevant secondary considerations include commercial success, long-felt but unsolved needs, failure of others, praise, and unexpected results. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007); *Institut Pasteur & Universite Pierre et Marie Curie v. Focarino*, 738 F.3d 1337, 1344 (Fed. Cir. 2013); *In re Soni*, 54 F.3d 746 (Fed. Cir. 1995). Secondary considerations are "not just a cumulative or confirmatory part of the obviousness

calculus but constitute [] independent evidence of nonobviousness . . . [and] enable [] the court to avert the trap of hindsight." *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013) (internal quotation marks and citations omitted). "This objective evidence must be 'considered as part of all the evidence, not just when the decisionmaker remains in doubt after reviewing the art.'" *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012) (internal citations omitted).

Patent Owner contends that the Examiner failed to credit the evidence of nonobviousness of the claimed invention. Appeal Br. 9–10. As evidence, Patent Owner cited studies performed with the Xience V stent. Patent Owner asserts that Xience V is a stent sold by Abbott Laboratories that "employs Solef® 21508 (Patent Owner's Response to ACP, at pg. 16), a VDF:HFP copolymer that comprises about 85% VDF and about 15% HFP." Appeal Br. 11.

Copying

Patent Owner states that the invention of the '844 Patent has been copied and adopted by others in the industry, including by Abbott (Xience V stent) and by Boston Scientific (Promus stent). Appeal Br. 9–10. As evidence, Patent Owner cites to paragraph 224 of the first Mikos declaration. However, paragraph 224 merely alleges copying by Abbott and Boston Scientific without factual evidence or analysis to support this statement. RAN 71. Consequently, without adequate evidence that Abbott and Boston Scientific copied the claimed invention, we give this argument little weight.

Commercial success

Patent Owner contends that commercial success of the claimed invention is demonstrated by the statement in Abbott's 2008 Form 10K that "'Xience V became the market-leading drug eluting stent in the U.S. in the fourth quarter of 2008,' within just three months of FDA approval" and Dr. Mikos's statement that the "PVDF-HFP coating used in the Xience V stent is an important factor in the clinical success of the Xience V stent, and therefore also in the commercial success of the Xience V and Promus stents. First Mikos Decl. ¶ 227. Patent Owner further cited Abbott's fact sheet on the Xience V stent which represented that "the composition of the polymer coating" in the Xience V stent "is important in overall clinical safety and efficacy outcomes." Appeal Br. 11 (fn. 4). Patent Owner also cited evidence that Xience's thin, nonreactive polymer accounted for its success. *Id.* at 12 (fn. 5).

For evidence of secondary considerations to be accorded substantial weight, there must be a nexus between the claimed invention and what is relied upon as the secondary consideration. *In re GPAC*, Inc., 57 F.3d 1573, 1580 (Fed. Cir. 1995). A nexus is established when the secondary consideration is attributed to a feature of the claimed invention. *Ormco Corp. v. Align Tech.*, Inc., 463 F.3d 1299, 1311–12.

In this case, even if there is evidence that the coating is one factor that contributed to the success of Xience, there is additional evidence that the drug and stent material are also important reasons for its success. Neither the drug nor the stent material is recited in claims 1 and 19. In this regard, as noted by the Examiner (RAN 73), Ex. 10 describes the drug and stent frame as reasons for the success of Xience V:

> Assessing why second-generation DES such as Xience may be superior to earlier-generation stents, the editorialists point out that they may differ on many fronts: the antiproliferative agent (in this case everolimus vs. paclitaxel), the polymer layer (Xience's is biocompatible), and stent frame (flexible cobalt-chromium vs. stainless steel). For example, improved stent design may result in better stent apposition and endothelialization as well as reduced platelet aggregation and thrombus formation. However, since the relative contribution of each of these elements to the enhanced performance of Xience is unknown, the study results are not necessarily applicable to other everolimus-eluting stents, Drs. Lange and Hillis caution.

Ex. 10

Similarly, Exhibit 9 states:

> Everolimus is a more potent drug than those used in the first-generation coated stents and also is contained in a thin, inert polymer that is less likely to cause inflammation, Stone said. The Xience stent itself is also thinner than the previous devices, he added.

Patent Owner represented that Dr. Stone had attributed Xience's commercial success to the polymer coating. Appeal Br. 12 (fn. 5). However, in theheart.org it was reported that Dr. Stone highlighted several reasons for the success of Xience, and not only the polymer coating as indicated by Patent Owner:

> Stone, who first presented the SPIRIT III results at the TCT 2007 meeting, told heartwire that two-year results will be presented at the upcoming EuroPCR meeting in Barcelona. He highlighted design characteristics of the Xience—**thinner struts; a thin, nonreactive polymer; and a drug with similar potency to sirolimus**—as key reasons not only for the reduced late loss at nine months, fewer repeat procedures at one year, and fewer procedural MIs, but also as factors that may ensure the stent also performs better over time.

theheart.org (emphasis added).

Thus, it has not been established that the claimed polymer in the 85:15 wt% ratio is responsible for the asserted success of the claimed invention, rather than

the drug or the stent material—both which are unclaimed features. Accordingly, the preponderance of the evidence does not support a nexus between commercial success and the merits of the claimed invention ("For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *GPAC*, 57 F.3d at 1580).

Unexpected results

A showing of "unexpected results" can be used to demonstrate the non-obviousness of the claimed invention. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("One way for a patent applicant to rebut a *prima facie* case of obviousness is to make a showing of 'unexpected results,' *i.e.*, to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected."). Those results must be "surprising or unexpected" to one of ordinary skill in the art when considered in the context of the closest prior art. *Soni*, 54 F.3d at 750; *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004) (A showing of "new and unexpected results" must be "relative to prior art."); *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) ("[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art"). To establish unexpected results, the claimed subject matter must be compared with the closest prior art. *Baxter*, 952 F.2d at 392.

Citing paragraph 25 of Dr. Mikos's first declaration, Patent Owner contends that "the PVDF-HFP coated Xience V stent is more thromboresistant (*i.e.*, shows greater tendency to reduce thrombus formation) than other drug-eluting stent

coatings." Appeal Br. 12. Patent Owner also contends that "numerous clinicians have also emphasized that the PVDF-HFP polymer used in the Xience V stent shows unexpectedly less inflammation," again citing to the Mikos declaration. *Id.*

Paragraph 227 of the Mikos declaration refers to Abbott's data in Exhibits 7 and 8. Exhibit 7 is undated. Exhibit 7 at ABT046618 shows that the weight of thrombus adhered to the stent for Xience V was less than for the Cypher, Endeavor, and Taxus Liberté stents. ABT046619 shows that Xience V had lower thrombus adherence "due to smooth coating integrity and hemocompatability of the XIENCE V Fluoropolymer" as compared to the Vision stent.

Dr. Mikos did not fully describe the coatings, stent materials, or therapeutic agents utilized in the stents to which the performance of Xience V was compared. Cypher comprises the drug sirolimus combined with a polymer blend of two non-erodible polymers, polyethylene-co-vinyl acetate (PEVA) and poly n-butyl methacrylate (PBMA), to form the basecoat. First Mikos Decl. ¶ 24. To establish unexpected results, the comparison must be against the closest prior art. *Baxter*, 952 F.2d at 392; *Iron Grip Barbell Co.*, 392 F.3d at 1322. Dr. Mikos did not establish that the coating on Cypher constitutes the closest prior art.

In addition to this, Dr. Mikos did not provide evidence that the purported improved results for Xience V was due to a claimed feature, rather than an unclaimed feature, such as the drug or stent material. *Ormco Corp,* 463 F.3d at 1311–12. Dr. Mikos also did not state the results would have been unexpected or surprising to one of ordinary skill in the art. *Soni*, 54 F.3d at 750.

Exhibit 8 was also cited by Dr. Mikos as evidence of unexpected results. Exhibit 8 is undated. Dr. Mikos cited page 28 of Exhibit 8. This page shoes that the average thrombus weight for Xience was less than for "Vision BMS." "BMS"

is a bare metal stent. Ex. 8, p. 28. The comparison therefore does not appear to be with the closest prior art since Tuch describes coated stents and Vision BMS is bare metal. Tuch1, Tuch3–6. *Baxter*, 952 F.2d at 392.

Dr. Mikos further testified in his written declaration that "numerous clinicians have also emphasized that the PVDF-HFP polymer used in the Xience V stent shows unexpectedly less inflammation." First Mikos Decl. ¶ 228. As evidence, Dr. Mikos cited Exhibits 9 and 10.

Exhibit 9 is a news article. The article mentions that Xience V is "less likely to cause inflammation." Exhibit 10 is also a news article. The article states:

> In a telephone interview with TCTMD, Robert S. Schwartz, MD, of the Minneapolis Heart Institute Foundation (Minneapolis, MN), underlined the role of the polymer in differentiating between the stent generations, saying that Taxus' older polymer was more likely to induce inflammation.

This evidence is not persuasive since it does not establish that the reduction in inflammation observed with Xience V is in comparison with the closest prior art as required under *Baxter*, 952 F.2d at 392. Rather, it appears the news articles are reporting that Xience's polymer is less inflammatory than the polymers on existing stents. Patent Owner has not provided sufficient testimony that this reduced inflammation would have been unexpected by one of ordinary skill in the art in comparison to the polymers described in Tuch, for example, which teaches stents with polymer coatings, including a homopolymer of VDF (Tuch6).

Consequently, the evidence does not support Dr. Mikos's opinion in paragraph 228 about unexpected results associated with the claimed polymer.

Industry praise

Patent Owner states that there "has been industry praise for Xience V that is attributable to the claimed invention." Appeal Br. 11.

We have reviewed Exhibits 6, 9, and 10, each of which describes success with Xience. However, as discussed above, it is not evident from these articles that the success and praise is a result of the claimed invention, rather than and unclaimed feature such as the drug or stent design. Exhibit 10, for example, compares Xience containing the everolimus drug in its coating with a paclitaxel stent. The article asks "'Should we abandon paclitaxel-eluting stents in favor of second-generation everolimus-eluting stents on the basis of the results of [this] study'," indicating that, at least in this case, the praise and success may be related to the everolimus drug.

SUMMARY

After considering the evidence in this record, including the evidence of secondary considerations and the declarations, we conclude that a preponderance of the evidence supports the Examiner's determination that claims 1 and 19 are unpatentable under 35 U.S.C. § 103(a) (pre-AIA) as obvious in view of Tuch, Tu, and Lo. Dependent claims 2–17 and 20–23 were not argued separately. We affirm the rejection of these claims for the reasons given by the Examiner.

TIME PERIOD FOR RESPONSE

In accordance with 37 C.F.R. § 41.79(a)(1), the "[p]arties to the appeal may file a request for rehearing of the decision within one month of the date of: . . . [t]he original decision of the Board under § 41.77(a)." A request for rehearing must be in compliance with 37 C.F.R. § 41.79(b). Comments in opposition to the

request and additional requests for rehearing must be in accordance with 37 C.F.R. § 41.79(c) & (d), respectively. Under 37 C.F.R. § 41.79(e), the times for requesting rehearing under paragraph (a) of this section, for requesting further rehearing under paragraph (d) of this section, and for submitting comments under paragraph (c) of this section may not be extended.

An appeal to the United States Court of Appeals for the Federal Circuit under 35 U.S.C. §§ 141–144 and 315 and 37 C.F.R. § 1.983 for an *inter partes* reexamination proceeding "commenced" on or after November 2, 2002 may not be taken "until all parties' rights to request rehearing have been exhausted, at which time the decision of the Board is final and appealable by any party to the appeal to the Board." 37 C.F.R. § 41.81. *See also* MPEP § 2682 (8th ed., Rev. 7, July 2008).

In the event neither party files a request for rehearing within the time provided in 37 C.F.R. § 41.79, and this decision becomes final and appealable under 37 C.F.R. § 41.81, a party seeking judicial review must timely serve notice on the Director of the United States Patent and Trademark Office. See 37 C.F.R. §§ 90.1 and 1.983.

AFFIRMED

Appeal 2014-008135
Reexamination Control 95/000,542 and 95/000,552
Patent 7,591,844 B2

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BOSTON SCIENTIFIC SCIMED and ABBOTT LABORATORIES
Requester and Respondent

v.

Patent of
CORDIS CORP., A JOHNSON & JOHNSON CO., and WYETH, A PFIZER CO.
Patent Owner and Appellant

Appeal 2014-008135
Reexamination Control 95/000,542 and 95/000,552
Patent 7,591,844 B2
Technology Center 3900

Before ROMULO H. DELMENDO, RICHARD M. LEBOVITZ, and JEFFREY B. ROBERTSON, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on the appeal by Patent Owner from the Patent Examiner's final rejection of claims 1–17 and 19–23 as obvious under 35 U.S.C. § 103 in the above-identified merged *inter partes* reexaminations of United States Patent

7,591,844 B2. The Board's jurisdiction for this appeal is under 35 U.S.C. §§ 6(b), 134, and 315 (pre-AIA). We affirm.

BACKGROUND

The patent in dispute in this appeal is US 7,591,844 B2 ("the '844 patent") which issued September 22, 2009. The real parties in interest and assignees are Cordis Corporation, a Johnson & Johnson company, and Wyeth, a Pfizer company ("Patent Owner"). Appeal Br. 1 (October 17, 2012). Patent Owner appeals the Examiner's final rejection of claims 1–17 and 19–23.

A request for *inter partes* reexamination of the '844 patent was filed April 15, 2010 by Boston Scientific SCIMED, Inc. under 35 U.S.C. §§ 311–318 and 37 C.F.R. §§ 1.902–1.997. A second request for *inter partes* reexamination was filed June 14, 2010 by Abbott Laboratories. The reexaminations were merged into a single proceeding. Decision, *Sua Sponte* Merging *inter partes* proceedings (Nov. 26, 2010).

An oral hearing was held January 21, 2015. A transcript of the hearing has been entered into the record ("Hearing Tr.").

The claimed subject matter of the '844 patent relates to a device for intraluminal implantation in a vessel comprising a "balloon expandable stent" and a "pharmaceutical agent-containing coating." The coating comprises vinylidinefluoride (VDF) copolymerized with hexafluoropropylene (HFP) in a weight percent ratio of 85:15. According to the '844 patent, transluminal angioplasty can be used to increase blood flow through a blocked artery by widening the artery through the use of an expandable balloon stent. '844, cols. 1–2. Although angioplasty has a short-term immediate benefit, the benefit is not always

lasting."Upon pressure expansion of an intracoronary balloon catheter during angioplasty, smooth muscle cells within the vessel wall become injured, initiating a thrombotic and inflammatory response." *Id.* at col. 2, ll. 10–13. As a result, the vascular wall can narrow again in a process called "restenosis." *Id.* at col. 1, ll. 46–51; col. 2, ll. 33–35. The '844 patent teaches that stent coatings containing a pharmaceutical agents may be used to reduced restenosis. *Id.* at col. 4, ll. 43–54. The patent teaches in the "Background of the Invention" that "[s]tents with coatings made from polyvinylidenefluoride [VDF] homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested." '844 patent, col. 5, ll. 4–6.

CLAIM 1

Independent claims 1 and 19 are the only independent claims involved in the appeal. Claim 1 is drawn to a device and claim 19 to a method of preparing a device. Claim 1 is representative and reads as follows (abbreviations within braces added):

> 1. A device for intraluminal implantation in a vessel comprising a balloon-expandable stent and a pharmaceutical agent-containing coating, said coating comprising a biocompatible polyfluoro copolymer that comprises about eighty-five weight percent vinylidinefluoride {VDF} copolymerized with about fifteen weight percent hexafluoropropylene {HFP} and at least one pharmaceutical agent intermixed with said copolymer, wherein said coating has not been subjected to a maximum temperature greater than 60° C during the coating process or afterward, thereby providing an adherent coating that remains adhered to the device upon expansion of the balloon-expandable stent.

REJECTIONS

The claims stand rejected by the Examiner over 33 different combinations of publications. Appeal Br. 4–6; Abbott Respondent Br. 1. Each of the rejections of independent claims 1 and 19 is based on substantially the same factual underpinnings, but relies on different publications for the same set of facts. Rather than addressing each ground separately, Patent Owner has focused its arguments on the factual basis of the rejections, grouping their arguments together for the various grounds of rejection of the independent claims. The rejections of the dependent claims were not argued separately.

For clarity, the table below summarizes the ten different grounds of rejection which involve independent claims 1 and 19. The rejections which involve dependent claims only have not been listed since they were not separately argued. There are three main groups of publications: 1) Tuch,[1] Wright, Kamath, and Patent Owner's Admissions, each of which is cited for teaching a stent coated with a polymer comprising a therapeutic agent: 2) Tu[2] and Lilenfeld, each of which is cited for teaching of a medical device comprising VDF:HFP; and 3) Lo[3], Wille, and Modern Fluoropolymer, each of which is cited for teaching of VDF:HFP in the claimed wt% of 85:15.

[1] Tuch	US 5,824,048	Oct. 20, 1998
[2] Tu et al. (Tu)	US 4,816,339	Mar. 28, 1989
[3] Lo	US 3,178,399	Apr. 13, 1965

	1	2	3	4	5	6	7	8	9	10
	1-17, 19-23	1-15,19-21	1-15, 19-21	1-15, 19-21	1-15,19-21	1-17, 19-23	1-17,19-23	1,2,8,19,20	1,2,8,19,20	1,2,8,19,20
Tuch		Y	Y	Y	Y					
Wright						Y	Y			
Kamath								Y	Y	Y
Pat. Admission	Y									
Tu	Y	Y		Y	Y	Y	Y	Y	Y	Y
Lilenfeld			Y							
Lo	Y	Y				Y		Y		
Wille				Y			Y		Y	
Modern Fluoropolymers					Y					Y

The table above shows the ten different grounds over the independent claims. Because the rejections were argued together, we have focused on the rejection based on Tuch, Tu, and Lo (rejection 2, above), and have not reached rejections 1 and 3–10, although as recognized by Patent Owner, similar rationale would apply.

In addition to the prior art publications, the following declarations have been cited as evidence:

First Declaration by Antonios G. Mikos, Ph.D ("First Mikos Decl.") dated Aug. 27, 2010. Dr. Mikos was a Professor of Bioengineering and Chemical and Biomolecular Engineering in the Departments of Bioengineering and Chemical and Biomolecular Engineering at Rice University at the time the declaration was executed. First Mikos Decl. ¶ 1. Dr. Mikos testified that he has expertise in the synthesis, fabrication and application of biomaterials, specifically polymers, for medical applications, including cardiovascular applications. *Id.* at ¶ 3. Dr. Mikos testified on behalf of the Patent Owner.

2012 Declaration by Michael N. Helmus, Ph.D. ("2012 Helmus Decl.") dated March 30, 2012. Dr. Helmus testified that he is an expert in biomaterials, biocompatibility, and biomaterial databases for medical device applications and currently works as a consult in the field of medical devices. Dr. Helmus testified on behalf of Abbott.

SCOPE AND CONTENT OF THE PRIOR ART[4]

Tuch

Tuch1. Tuch describes an intravascular stent that has a coating on its tissue-contacting surface which comprises a polymer and therapeutic substance. Tuch, col. 2, ll. 36–38.

Tuch2. Tuch teaches that the stent can be of any design, including self-expanding and balloon-expandable types. *Id.* at col. 4, ll. 10–13.

Tuch3. Tuch discloses that the polymer must be biocompatible and minimize irritation to the vessel wall when the stent is implanted. *Id.* at col. 5, ll. 14–16.

Tuch4. Tuch also teaches that the polymer may be either biostable or bioabsorbable. *Id.* at col. 5, ll. 15–16.

Tuch5. Tuch describes "biostable polymers with a relatively low chronic tissue response." *Id.* at col. 5, ll. 33–34.

Tuch6. The list of the biostable polymers includes "vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride [VDF] and polyvinylidene chloride." *Id.* at col. 5, ll. 38–42.

Tuch7. Tuch teaches that during implantation of an expandable stent, the delivery balloon expands and deforms the stent elements and coating. *Id.* at col. 7, ll. 9–11.

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[4] Factual considerations that underlie the obviousness inquiry include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

Tuch8. When the polymeric overlayer on the stent is uniform and "made with materials which have little elasticity," Tuch teaches that "the overlayer can sustain significant cracking during such deformation" and the "cracks can then act as channels for more rapid elution of drugs from the drug-rich base coating." *Id.* at col. 7, ll. 11–15.

Tuch9. Tuch teaches that "cracking of the overlayer can be reduced and drug elution times increased by providing a porous overlayer on the stent." *Id.* at col. 7, ll. 16–18.

Tuch10. Tuch teaches that the coating should be "resilient"[5] for stent expansion: "The inclusion of a polymer in intimate contact with a drug on the stent allows the drug to be retained on the stent in a resilient matrix during expansion of the stent . . ." *Id.* at 2:42–46. In context, Tuch uses the term "resilient" to have its ordinary meaning, which is to be "able to return to an original shape after being pulled, stretched, pressed, bent, etc.," a synonym being "elastic."

Tu

Tu1. Tu describes implantable biomedical devices formed with layers of polytetrafluoroethylene, polytetrafluoroethylene/elastomer, and elastomer. Tu, col 2, ll. 7–37.

Tu2. Tu teaches that its invention relates to various types of implantable bioomedical devices, including heart valve leaflets, and the invention particularly relates to vascular grafts. *Id.* at col. 1, ll. 27–32; col. 2, ll. 36–40.

[5] "Resilient" means "able to return to an original shape after being pulled, stretched, pressed, bent, etc." and a synonym is "elastic." http://www.merriam-webster.com/dictionary/resilient (accessed Jan. 28, 2015).

Tu3. Tu discloses a list of compounds used to prepare the elastomer. *Id.* at col. 2, ll. 20–30. Polyvinylidene fluoride co-hexafluoropropylene (VDF:HFP) is first on the list. *Id.* at col. 2, ll. 23–24.

Tu4. Tu teaches that the elastomer provides elasticity and strength. *Id.* at col. 3, ll. 40–44, 64.

Tu5. According to Tu, the "elastomer solution may optionally contain therapeutic agents including but not limited to antibiotic and/or hemostatic substances." *Id.* at col. 8, ll. 45–47.

Tu6. Tu teaches that the implantable material made of polytetrafluoroethylene and elastomer is biologically compatible. Id. at col. 2, ll. 11–19, 31; col. 3, l.

Lo

Lo1. Lo describes copolymers of vinylidene fluoride (VDF) and hexafluoropropene (HFP) which have flexibility, elasticity, and extensibility. Lo, col. 2, ll. 33–36, 47, and 56–58.

Lo2. Figure 1 of Lo shows an increase of tensile PSIG and reversible elongation from about 86 mol percent to a maximum of about 94 mol percent with a copolymer made of vinylidene fluoride and hexafluropropene.

Lo3. Lo teaches that "[a]bove about 94 mol percent vinylidene fluoride (i.e. less than 6 mol percent hexafluoropropene) the copolymer is essentially crystalline in nature and the reversible elongation decreases rapidly." Lo, col. 9, ll. 33–36.

Lo4. The Examiner found that "copolymers with an optimal combination of tensile strength and reverse elongation are achieved at 93 mol % VDF, corresponding to a VDF/HFP wt% ratio of 85:15 (Fig. 1; col. 9, lines 15–27)."

RAN 14. Dr. Mikos in his declaration acknowledged that "Lo describes VDF/HFP coatings having VDF:HFP weight percent of 85: 15." First Mikos Decl. ¶ 41.

Le Morel[6]

LeM1. LeMorel teaches implants such as stents. LeMorel 2:4–15.

LeM2. Le Morel teaches that the substrate of the implant can be a polymer, and specifically identifies copolymers of vinylidene fluoride and hexafluorpropylene among a list. *Id.* at 3:1–5 and 18–19.

LeM3. Le Morel teaches in the case of stents, a fluorinated polymer is advantageous. *Id.* at 4:4–10.

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE PRIOR ART

The Examiner found that Tuch describes a balloon-expandable stent having a coating containing a therapeutic agent, meeting the claimed limitation of "a balloon-expandable stent and a pharmaceutical agent-containing coating." RAN 13-14; Tuch1–2, 7. The Examiner found that the coating may be formed with VDF. RAN 14; Tuch6. The Examiner found that Tuch does not describe a coating "that comprises about eighty-five weight percent vinylidinefluoride [VDF] copolymerized with about fifteen weight percent hexafluoropropylene [HFP]," but found that Lo describes such a copolymer coating and its advantages with respect tensile strength and reversible elongation. RAN 14; Lo1–4. Furthermore, the

[6] Le Morel et al. (Le Morel or LeM) FR 2,785,812 Nov. 16, 1998. Citations to translation of record.

Examiner found that Tu demonstrates the biocompatibility of VDF/HFP polymers and that such copolymers can contain therapeutic substances. RAN 14; Tu5.

Based on the teachings of Lo and Tu, the Examiner determined it would have been obvious to one of ordinary skill in the art to have replaced "Tuch's crystalline VDF homopolymer with the partially crystalline copolymers having a VDF/HFP wt % ratio of about 85:15 (as recited in [device] claim 1 and method claim 19) . . . to arrive [at] the instant invention." RAN 14–15. The Examiner's rationale was that a person of ordinary skill in the art would have understood that VDF/HFP is advantageous as compared to VDF homopolymers and has optimal tensile strength and reversible elongation at VDF/HFP wt% ratio of 85:15 as shown by Lo. *Id.* at 14.

Discussion

Patent Owner contends that the Examiner erred in combining the publications to have arrived at the claimed invention. Specifically, Patent Owner argues that one of ordinary skill in the art reading Tuch would not have had reason to choose polymers from publications other than Tuch because Tuch did not identify a problem with its polymers used for its drug coating layer. Appeal Br. 16. Patent Owner also argues that it is improper to combine Tu's teachings with those of Tuch. *Id.* at 17.

Choice of VDF:HFP

It is unnecessary that Tuch disclose any shortcomings in its list of polymers for the ordinary skilled worker to have found it obvious to have employed an alternative polymer for its coating since it is obvious to use a prior art element for

its established function. As held in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007), in making an obviousness determination, it must be asked "whether the improvement is more than the predictable use of prior art elements according to their established functions." Thus, even if Tuch did not disclose a problem with its polymers, one of ordinary skill in the art would have found it obvious to have employed the known polymers of Tu and Lo for their known and expected properties. As argued by Abbott, Abbott Respondent Br. 12, the reason to combine could be provided by the "normal desire of scientists or artisans to improve upon what is already generally known." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003).

In addition to this, Tuch does not limit its polymers to those specifically disclosed. Tuch teaches using "vinyl halide polymers and copolymers," and specifically discloses "polyvinylidene halides, such as polyvinylidene fluoride." Tuch6. This disclosure, while mentioning a specific polyvinylidene halide, also includes broader classes ("vinyl halides" and "polyvinylidene halides"), including copolymers, which would have reasonably suggested that additional polymers, outside those specifically described in Tuch, would be useful as Tuch's polymer coating comprising a therapeutic substance.

To support their position about the unobviousness of using polymers other than those disclosed in Tuch, Patent Owner cites *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342,1370–71 (Fed. Cir. 2012).

> As in *Kinetic Concepts, Inc.* 688 F.3d at 1369, a case in which the Federal Circuit overturned a prior finding of obviousness, the record here "is devoid of any reason someone would combine [the cited] references." Where, as here, each device that the references describe "independently operates effectively," a person having ordinary skill in

> the art "would have no reason" to combine the reference" respective teachings. *Id.*

Appeal Br. 17. *See* also Rebuttal Br. 3.

In *Kinetic*, the issue was whether to combine publications which "both . . . independently accomplish similar functions, namely, draining fluids." *Kinetic Concepts, Inc.* 688 F.3d at 1369. One set of publications involved negative pressure to drain wounds. *Id.* at 1362-1363. The other set of publications disclosed a different type of wound drainage system. *Id.* at 1365. The obviousness rejection was predicated on combining the two sets of publications to meet a limitation in the claim of using negative pressure to treat a wound, where wound treatment had not been found to be present in the negative pressure publications. *Id.* at 1361, 1363. Because each publication was complete in teaching a wound drainage method, and there was no teaching that negative pressure could be used to treat wounds, the court found "a person having ordinary skill in the art, who was merely seeking to create a better device to drain fluids from a wound, would have no reason to combine the features of both devices into a single device." *Id.* at 1369.

The facts of this case are clearly distinguishable. Tuch teaches various polymer coatings for its stent, including broad classes that encompass unnamed species. Tu was cited in the rejection for teaching polymers suitable for Tuch's stent coating. The reason to consult Tu is because Tuch's list of polymers is clearly not exhaustive in view of Tuch's description of broad classes of polymers, such as vinyl halide polymers and copolymers, and polyvinylidene halides. Tuch6. Tuch also uses the transitional phrase "such as" in prefacing the list of biostable polymers and in reciting specific examples of the broader classes, indicating that Tuch did not confine the skilled worker to the explicit list, but contemplated

polymers outside of it. ("Also, biostable polymers with a relatively low chronic tissue response such as . . . and other polymers could also be used if they can be dissolved and cured or polymerized on the stent such as . . . vinyl halide polymers and copolymers, such as . . . " Tuch, col. 5, ll. 33–39).

Patent Owner argues that Tuch recites a long laundry list of polymers and therefore would not have directed the skilled worker to the specifically claimed polymers. Appeal Br. 24. First Mikos Decl. ¶¶ 52–56.

The fact that "vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride [VDF] and polyvinylidene chloride" appear in a longer list (Tuch6) would not have dissuaded one of ordinary skill from choosing VDF copolymers. The list recited in Tuch is of polymers that Tuch considered useful for its stent coating and therefore is a disclosure of each and every one for a stent coating. There does not have to be a working example of vinyl halide polymer copolymer, polyvinylidene halide, or VDF, as alleged by Dr. Mikos (First Mikos Decl. ¶ 143) for one of ordinary skill in the art to have recognized such compounds as useful for a polymer coating since Tuch expressly describes their use for this purpose. Tuch6.

Furthermore, Patent Owner admitted in the "Background" of the '844 patent that "[s]tents with coatings made from polyvinylidenefluoride homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested." '844 patent, col. 5, ll. 4–6. *See* also "Preexamination Search Statement and Accelerated Examination Support Document" 12 ("AESD"; filed Nov. 16, 2007 in the application that led to the '844 patent) identifying the latter statement as prior art.

Dr. Mikos attempts to distinguish Tuch because Tuch describe a porous overlayer of polymer to control drug release. First Mikos Decl. ¶ 144. However, the claim does not exclude such a porous layer made of VDF:HFP.

Patent Owner also argues that the stent coating in Tuch is in contact with the vessel wall lining and in contact with blood, while in Tu, the graft's inner surface which contacts the blood lacks the elastomer. Appeal Br. 23. While this might be the case, Tu teaches that it's the polytetrafluoroethylene/elastomer which can be used generally in other medical devices, such as a heart valve leaflet that could be in contact with blood. Tu2.

Is there an adequate reason to have combined Tuch and Tu?

Patent Owner argues that the record is devoid of reason to have combined Tuch and Tu. Appeal Br. 17. Patent Owner also argues that Tu relates to vascular grafts and therefore is not relevant to Tuch.[7] *Id.* at 18:1–2.

A preponderance of the evidence does not support Patent Owner's position that the record lacks a reason to combine Tuch with Tu.

First, Tu is not limited to vascular grafts, but clearly teaches that its polymers are useful for various types of implantable devices. Tu2. While vascular grafts are preferred, such preference does not negate the broader teaching.

Second, Tu's polyvinylidene fluoride co-hexafluoropropylene has the properties described in Tuch as useful for its stent coating. These properties are discussed below:

1) Tuch's polymers are biocompatible as they are in Tu. Tuch3; Tu6.

[7] Taking a contrary position, in the AESD filed in the application that led to the '844 patent, Patent Owner characterized Tu (US 5,061,276) as one of the "most closely related" prior art references. AESD 6. Abbott Respondent Br. 15.

2) Tuch teaches elastic polymers are beneficial for coatings in expandable stents. Tuch8, 10. Tu's elastomers are elastic. Tu4.

Patent Owner contends that elasticity would not have been a factor in choosing a polymer coating for Tuch's stent. Appeal Br. 18–19. However, Tuch teaches that, when the stent delivery balloon expands, the stent coating can deform. Tuch7. When materials are used for the polymers which "have little elasticity," the polymer overlayer can crack during the expansion and result in rapid drug elution. Tuch8. Tuch teaches one way to reduce the cracking. Tuch9. Since Tuch teaches a problem with cracking when materials having little elasticity are utilized in the polymer layer, one of ordinary skill in the art would have reasonably sought materials with high elasticity to avoid the problem when the stent is expanded.

Furthermore, Tuch teaches that using a resilient matrix during expansion of the stent is beneficial for drug retention. Tuch10. Resilient is a synonym for elastic. Fn. 5. *See* also 2012 Helmus Decl. ¶ 6 for further evidence of the desirability of an elastic polymer. Tu teaches elastomers that provide elasticity and strength. Tu4.

Dr. Mikos testified that the "physical and mechanical properties that are important for the Tu vascular grafts . . . are very different from the physical and mechanical properties that are important for polymer coatings used on balloon expandable stents [as in Tuch]." First Mikos Decl. ¶ 43. Dr. Mikos identifies elasticity as important in vascular grafts. *Id.* at ¶ 44. Dr. Mikos, however, did not explain how elasticity is distinguishable from the ability of a polymer to be elongated or deformed before breaking which he identified as an "important property" of a stent polymer coating. *Id.* at ¶¶ 46, 147. That is, while Tu's graft may have a different purpose than Tuch's stent, Dr. Mikos admits that a stent

coating must be resilient (resist deformation before breaking) which is the same property that Dr, Mikos identifies as important in vascular grafts. Consequently, Dr. Mikos's testimony about the lack of reason to combine Tuch and Tu is not supported by persuasive factual evidence.

3) Tuch teaches that polyvinylidene fluoride is a useful polymer for its coating comprising a therapeutic substance. Tuch1, 6. The first elastomer on Tu's list is a copolymer comprising polyvinylidene fluoride and hexafluoropropylene (VDF:HFP). Tu3. The obviousness of choosing VDF:HFP as a stent coating is further evidenced by Le Morel who describes the copolymer as coating on a stent. LeM1–3.

4) Tuch teaches a polymer coating that delivers a therapeutic substance. Tuch1. Tu also teaches that its elastomer can contain therapeutic agents. Tu5.

Summary

In sum, a preponderance of the evidence supports the determination it would have been obvious to have selected VDF:HFP from Tu as the polymer coating in Tuch. Contrary to Patent Owner's statement that it would have been a scavenger hunt to find VDF:HFP (Hearing Tr. 4:6–11), VDF:HFP is disclosed by Tu as a useful elastomer for an implantable medical device and Tu's elastomers have the properties described by Tuch as advantageous in a stent, which is an example of an implantable device.

Proportion of VDF and HFP

As far as the 85:15 copolymer of VDF and HFP recited in the claims, Lo teaches that a 85:15 copolymer is advantageous with respect to flexibility,

elasticity, extensibility, tensile strength, and reverse elongation. Lo1–4; RAN 14. One of ordinary skill in the art would have been motivated to have used Lo's polymer having these advantageous properties as the coating in Tuch because Tuch teaches a problem with coatings with low elasticity (Tuch8-9).

Because VDF:HFP is expressly described by Tu as useful for an implantable medical device (Tu2), the skilled worker would have reasonably consulted Lo to determine the optimal concentrations for each component, even if Lo does not teach the use of VDF:HFP for medical implants. Patent Owner's argument that Lo's uses are industrial and therefore not pertinent to stents (Appeal Br. 24; First Mikos Decl. ¶¶ 41–42) is unavailing since Lo was cited for teaching the properties of VDF:HFP which had been taught to be useful by Tu in a medical device.

Patent Owner's argument that VDF:HFP is not described as a carrier for a drug has little merit. Appeal Br. 25. As mentioned, Tu teaches that its elastomer may contain therapeutic agents. Tu5.

SECONDARY CONSIDERATIONS

Factual considerations that underlie the obviousness inquiry include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations. *Graham.*, 383 U.S. at 17-18. Relevant secondary considerations include commercial success, long-felt but unsolved needs, failure of others, praise, and unexpected results. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007); *Institut Pasteur & Universite Pierre et Marie Curie v. Focarino*, 738 F.3d 1337, 1344 (Fed. Cir. 2013); *In re Soni*, 54 F.3d 746 (Fed. Cir. 1995). Secondary considerations are "not just a cumulative or confirmatory part of the obviousness

calculus but constitute [] independent evidence of nonobviousness . . . [and] enable [] the court to avert the trap of hindsight." *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013) (internal quotation marks and citations omitted). "This objective evidence must be 'considered as part of all the evidence, not just when the decisionmaker remains in doubt after reviewing the art.'" *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012) (internal citations omitted).

Patent Owner contends that the Examiner failed to credit the evidence of nonobviousness of the claimed invention. Appeal Br. 9–10. As evidence, Patent Owner cited studies performed with the Xience V stent. Patent Owner asserts that Xience V is a stent sold by Abbott Laboratories that "employs Solef® 21508 (Patent Owner's Response to ACP, at pg. 16), a VDF:HFP copolymer that comprises about 85% VDF and about 15% HFP." Appeal Br. 11.

Copying

Patent Owner states that the invention of the '844 Patent has been copied and adopted by others in the industry, including by Abbott (Xience V stent) and by Boston Scientific (Promus stent). Appeal Br. 9–10. As evidence, Patent Owner cites to paragraph 224 of the first Mikos declaration. However, paragraph 224 merely alleges copying by Abbott and Boston Scientific without factual evidence or analysis to support this statement. RAN 71. Consequently, without adequate evidence that Abbott and Boston Scientific copied the claimed invention, we give this argument little weight.

Commercial success

Patent Owner contends that commercial success of the claimed invention is demonstrated by the statement in Abbott's 2008 Form 10K that "'Xience V became the market-leading drug eluting stent in the U.S. in the fourth quarter of 2008,' within just three months of FDA approval" and Dr. Mikos's statement that the "PVDF-HFP coating used in the Xience V stent is an important factor in the clinical success of the Xience V stent, and therefore also in the commercial success of the Xience V and Promus stents. First Mikos Decl. ¶ 227. Patent Owner further cited Abbott's fact sheet on the Xience V stent which represented that "the composition of the polymer coating" in the Xience V stent "is important in overall clinical safety and efficacy outcomes." Appeal Br. 11 (fn. 4). Patent Owner also cited evidence that Xience's thin, nonreactive polymer accounted for its success. *Id.* at 12 (fn. 5).

For evidence of secondary considerations to be accorded substantial weight, there must be a nexus between the claimed invention and what is relied upon as the secondary consideration. *In re GPAC*, Inc., 57 F.3d 1573, 1580 (Fed. Cir. 1995). A nexus is established when the secondary consideration is attributed to a feature of the claimed invention. *Ormco Corp. v. Align Tech.*, Inc., 463 F.3d 1299, 1311–12.

In this case, even if there is evidence that the coating is one factor that contributed to the success of Xience, there is additional evidence that the drug and stent material are also important reasons for its success. Neither the drug nor the stent material is recited in claims 1 and 19. In this regard, as noted by the Examiner (RAN 73), Ex. 10 describes the drug and stent frame as reasons for the success of Xience V:

> Assessing why second-generation DES such as Xience may be superior to earlier-generation stents, the editorialists point out that they may differ on many fronts: the antiproliferative agent (in this case everolimus vs. paclitaxel), the polymer layer (Xience's is biocompatible), and stent frame (flexible cobalt-chromium vs. stainless steel). For example, improved stent design may result in better stent apposition and endothelialization as well as reduced platelet aggregation and thrombus formation. However, since the relative contribution of each of these elements to the enhanced performance of Xience is unknown, the study results are not necessarily applicable to other everolimus-eluting stents, Drs. Lange and Hillis caution.

Ex. 10

> Similarly, Exhibit 9 states:
>
> Everolimus is a more potent drug than those used in the first-generation coated stents and also is contained in a thin, inert polymer that is less likely to cause inflammation, Stone said. The Xience stent itself is also thinner than the previous devices, he added.

Patent Owner represented that Dr. Stone had attributed Xience's commercial success to the polymer coating. Appeal Br. 12 (fn. 5). However, in theheart.org it was reported that Dr. Stone highlighted several reasons for the success of Xience, and not only the polymer coating as indicated by Patent Owner:

> Stone, who first presented the SPIRIT III results at the TCT 2007 meeting, told heartwire that two-year results will be presented at the upcoming EuroPCR meeting in Barcelona. He highlighted design characteristics of the Xience—**thinner struts; a thin, nonreactive polymer; and a drug with similar potency to sirolimus**—as key reasons not only for the reduced late loss at nine months, fewer repeat procedures at one year, and fewer procedural MIs, but also as factors that may ensure the stent also performs better over time.

theheart.org (emphasis added).

Thus, it has not been established that the claimed polymer in the 85:15 wt% ratio is responsible for the asserted success of the claimed invention, rather than

the drug or the stent material—both which are unclaimed features. Accordingly, the preponderance of the evidence does not support a nexus between commercial success and the merits of the claimed invention ("For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *GPAC*, 57 F.3d at 1580).

Unexpected results

A showing of "unexpected results" can be used to demonstrate the non-obviousness of the claimed invention. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("One way for a patent applicant to rebut a *prima facie* case of obviousness is to make a showing of 'unexpected results,' *i.e.,* to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected."). Those results must be "surprising or unexpected" to one of ordinary skill in the art when considered in the context of the closest prior art. *Soni*, 54 F.3d at 750; *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004) (A showing of "new and unexpected results" must be "relative to prior art."); *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) ("[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art"). To establish unexpected results, the claimed subject matter must be compared with the closest prior art. *Baxter*, 952 F.2d at 392.

Citing paragraph 25 of Dr. Mikos's first declaration, Patent Owner contends that "the PVDF-HFP coated Xience V stent is more thromboresistant (*i.e.,* shows greater tendency to reduce thrombus formation) than other drug-eluting stent

coatings." Appeal Br. 12. Patent Owner also contends that "numerous clinicians have also emphasized that the PVDF-HFP polymer used in the Xience V stent shows unexpectedly less inflammation," again citing to the Mikos declaration. *Id.*

Paragraph 227 of the Mikos declaration refers to Abbott's data in Exhibits 7 and 8. Exhibit 7 is undated. Exhibit 7 at ABT046618 shows that the weight of thrombus adhered to the stent for Xience V was less than for the Cypher, Endeavor, and Taxus Liberté stents. ABT046619 shows that Xience V had lower thrombus adherence "due to smooth coating integrity and hemocompatability of the XIENCE V Fluoropolymer" as compared to the Vision stent.

Dr. Mikos did not fully describe the coatings, stent materials, or therapeutic agents utilized in the stents to which the performance of Xience V was compared. Cypher comprises the drug sirolimus combined with a polymer blend of two non-erodible polymers, polyethylene-co-vinyl acetate (PEVA) and poly n-butyl methacrylate (PBMA), to form the basecoat. First Mikos Decl. ¶ 24. To establish unexpected results, the comparison must be against the closest prior art. *Baxter*, 952 F.2d at 392; *Iron Grip Barbell Co.*, 392 F.3d at 1322. Dr. Mikos did not establish that the coating on Cypher constitutes the closest prior art.

In addition to this, Dr. Mikos did not provide evidence that the purported improved results for Xience V was due to a claimed feature, rather than an unclaimed feature, such as the drug or stent material. *Ormco Corp,* 463 F.3d at 1311–12. Dr. Mikos also did not state the results would have been unexpected or surprising to one of ordinary skill in the art. *Soni*, 54 F.3d at 750.

Exhibit 8 was also cited by Dr. Mikos as evidence of unexpected results. Exhibit 8 is undated. Dr. Mikos cited page 28 of Exhibit 8. This page shoes that the average thrombus weight for Xience was less than for "Vision BMS." "BMS"

is a bare metal stent. Ex. 8, p. 28. The comparison therefore does not appear to be with the closest prior art since Tuch describes coated stents and Vision BMS is bare metal. Tuch1, Tuch3–6. *Baxter*, 952 F.2d at 392.

Dr. Mikos further testified in his written declaration that "numerous clinicians have also emphasized that the PVDF-HFP polymer used in the Xience V stent shows unexpectedly less inflammation." First Mikos Decl. ¶ 228. As evidence, Dr. Mikos cited Exhibits 9 and 10.

Exhibit 9 is a news article. The article mentions that Xience V is "less likely to cause inflammation." Exhibit 10 is also a news article. The article states:

> In a telephone interview with TCTMD, Robert S. Schwartz, MD, of the Minneapolis Heart Institute Foundation (Minneapolis, MN), underlined the role of the polymer in differentiating between the stent generations, saying that Taxus' older polymer was more likely to induce inflammation.

This evidence is not persuasive since it does not establish that the reduction in inflammation observed with Xience V is in comparison with the closest prior art as required under *Baxter*, 952 F.2d at 392. Rather, it appears the news articles are reporting that Xience's polymer is less inflammatory than the polymers on existing stents. Patent Owner has not provided sufficient testimony that this reduced inflammation would have been unexpected by one of ordinary skill in the art in comparison to the polymers described in Tuch, for example, which teaches stents with polymer coatings, including a homopolymer of VDF (Tuch6).

Consequently, the evidence does not support Dr. Mikos's opinion in paragraph 228 about unexpected results associated with the claimed polymer.

Industry praise

Patent Owner states that there "has been industry praise for Xience V that is attributable to the claimed invention." Appeal Br. 11.

We have reviewed Exhibits 6, 9, and 10, each of which describes success with Xience. However, as discussed above, it is not evident from these articles that the success and praise is a result of the claimed invention, rather than and unclaimed feature such as the drug or stent design. Exhibit 10, for example, compares Xience containing the everolimus drug in its coating with a paclitaxel stent. The article asks "'Should we abandon paclitaxel-eluting stents in favor of second-generation everolimus-eluting stents on the basis of the results of [this] study'," indicating that, at least in this case, the praise and success may be related to the everolimus drug.

SUMMARY

After considering the evidence in this record, including the evidence of secondary considerations and the declarations, we conclude that a preponderance of the evidence supports the Examiner's determination that claims 1 and 19 are unpatentable under 35 U.S.C. § 103(a) (pre-AIA) as obvious in view of Tuch, Tu, and Lo. Dependent claims 2–17 and 20–23 were not argued separately. We affirm the rejection of these claims for the reasons given by the Examiner.

TIME PERIOD FOR RESPONSE

In accordance with 37 C.F.R. § 41.79(a)(1), the "[p]arties to the appeal may file a request for rehearing of the decision within one month of the date of: . . . [t]he original decision of the Board under § 41.77(a)." A request for rehearing must be in compliance with 37 C.F.R. § 41.79(b). Comments in opposition to the

request and additional requests for rehearing must be in accordance with 37 C.F.R. § 41.79(c) & (d), respectively. Under 37 C.F.R. § 41.79(e), the times for requesting rehearing under paragraph (a) of this section, for requesting further rehearing under paragraph (d) of this section, and for submitting comments under paragraph (c) of this section may not be extended.

An appeal to the United States Court of Appeals for the Federal Circuit under 35 U.S.C. §§ 141–144 and 315 and 37 C.F.R. § 1.983 for an *inter partes* reexamination proceeding "commenced" on or after November 2, 2002 may not be taken "until all parties' rights to request rehearing have been exhausted, at which time the decision of the Board is final and appealable by any party to the appeal to the Board." 37 C.F.R. § 41.81. *See also* MPEP § 2682 (8th ed., Rev. 7, July 2008).

In the event neither party files a request for rehearing within the time provided in 37 C.F.R. § 41.79, and this decision becomes final and appealable under 37 C.F.R. § 41.81, a party seeking judicial review must timely serve notice on the Director of the United States Patent and Trademark Office. See 37 C.F.R. §§ 90.1 and 1.983.

AFFIRMED

Appeal 2014-008135
Reexamination Control 95/000,542 and 95/000,552
Patent 7,591,844 B2

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BOSTON SCIENTIFIC SCIMED and ABBOTT LABORATORIES
Requester and Respondent

v.

Patent of
CORDIS CORP., A JOHNSON & JOHNSON CO., and WYETH, A PFIZER CO.
Patent Owner and Appellant

Appeal 2014-008135
Reexamination Control 95/000,542 and 95/000,552
Patent 7,591,844 B2
Technology Center 3900

Before ROMULO H. DELMENDO, RICHARD M. LEBOVITZ, and JEFFREY B. ROBERTSON, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on the appeal by Patent Owner from the Patent Examiner's final rejection of claims 1–17 and 19–23 as obvious under 35 U.S.C. § 103 in the above-identified merged *inter partes* reexaminations of United States Patent

7,591,844 B2. The Board's jurisdiction for this appeal is under 35 U.S.C. §§ 6(b), 134, and 315 (pre-AIA). We affirm.

BACKGROUND

The patent in dispute in this appeal is US 7,591,844 B2 ("the '844 patent") which issued September 22, 2009. The real parties in interest and assignees are Cordis Corporation, a Johnson & Johnson company, and Wyeth, a Pfizer company ("Patent Owner"). Appeal Br. 1 (October 17, 2012). Patent Owner appeals the Examiner's final rejection of claims 1–17 and 19–23.

A request for *inter partes* reexamination of the '844 patent was filed April 15, 2010 by Boston Scientific SCIMED, Inc. under 35 U.S.C. §§ 311–318 and 37 C.F.R. §§ 1.902–1.997. A second request for *inter partes* reexamination was filed June 14, 2010 by Abbott Laboratories. The reexaminations were merged into a single proceeding. Decision, *Sua Sponte* Merging *inter partes* proceedings (Nov. 26, 2010).

An oral hearing was held January 21, 2015. A transcript of the hearing has been entered into the record ("Hearing Tr.").

The claimed subject matter of the '844 patent relates to a device for intraluminal implantation in a vessel comprising a "balloon expandable stent" and a "pharmaceutical agent-containing coating." The coating comprises vinylidinefluoride (VDF) copolymerized with hexafluoropropylene (HFP) in a weight percent ratio of 85:15. According to the '844 patent, transluminal angioplasty can be used to increase blood flow through a blocked artery by widening the artery through the use of an expandable balloon stent. '844, cols. 1–2. Although angioplasty has a short-term immediate benefit, the benefit is not always

lasting."Upon pressure expansion of an intracoronary balloon catheter during angioplasty, smooth muscle cells within the vessel wall become injured, initiating a thrombotic and inflammatory response." *Id.* at col. 2, ll. 10–13. As a result, the vascular wall can narrow again in a process called "restenosis." *Id.* at col. 1, ll. 46–51; col. 2, ll. 33–35. The '844 patent teaches that stent coatings containing a pharmaceutical agents may be used to reduced restenosis. *Id.* at col. 4, ll. 43–54. The patent teaches in the "Background of the Invention" that "[s]tents with coatings made from polyvinylidenefluoride [VDF] homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested." '844 patent, col. 5, ll. 4–6.

CLAIM 1

Independent claims 1 and 19 are the only independent claims involved in the appeal. Claim 1 is drawn to a device and claim 19 to a method of preparing a device. Claim 1 is representative and reads as follows (abbreviations within braces added):

> 1. A device for intraluminal implantation in a vessel comprising a balloon-expandable stent and a pharmaceutical agent-containing coating, said coating comprising a biocompatible polyfluoro copolymer that comprises about eighty-five weight percent vinylidinefluoride {VDF} copolymerized with about fifteen weight percent hexafluoropropylene {HFP} and at least one pharmaceutical agent intermixed with said copolymer, wherein said coating has not been subjected to a maximum temperature greater than 60° C during the coating process or afterward, thereby providing an adherent coating that remains adhered to the device upon expansion of the balloon-expandable stent.

REJECTIONS

The claims stand rejected by the Examiner over 33 different combinations of publications. Appeal Br. 4–6; Abbott Respondent Br. 1. Each of the rejections of independent claims 1 and 19 is based on substantially the same factual underpinnings, but relies on different publications for the same set of facts. Rather than addressing each ground separately, Patent Owner has focused its arguments on the factual basis of the rejections, grouping their arguments together for the various grounds of rejection of the independent claims. The rejections of the dependent claims were not argued separately.

For clarity, the table below summarizes the ten different grounds of rejection which involve independent claims 1 and 19. The rejections which involve dependent claims only have not been listed since they were not separately argued. There are three main groups of publications: 1) Tuch,[1] Wright, Kamath, and Patent Owner's Admissions, each of which is cited for teaching a stent coated with a polymer comprising a therapeutic agent: 2) Tu[2] and Lilenfeld, each of which is cited for teaching of a medical device comprising VDF:HFP; and 3) Lo[3], Wille, and Modern Fluoropolymer, each of which is cited for teaching of VDF:HFP in the claimed wt% of 85:15.

[1] Tuch	US 5,824,048	Oct. 20, 1998
[2] Tu et al. (Tu)	US 4,816,339	Mar. 28, 1989
[3] Lo	US 3,178,399	Apr. 13, 1965

	1	2	3	4	5	6	7	8	9	10
	1-17, 19-23	1-15,19-21	1-15, 19-21	1-15, 19-21	1-15,19-21	1-17, 19-23	1-17,19-23	1,2,8,19,20	1,2,8,19,20	1,2,8,19,20
Tuch		Y	Y	Y	Y					
Wright						Y	Y			
Kamath								Y	Y	Y
Pat. Admission	Y									
Tu	Y	Y		Y	Y	Y	Y	Y	Y	Y
Lilenfeld			Y							
Lo	Y	Y				Y		Y		
Wille				Y			Y		Y	
Modern Fluoropolymers					Y					Y

The table above shows the ten different grounds over the independent claims. Because the rejections were argued together, we have focused on the rejection based on Tuch, Tu, and Lo (rejection 2, above), and have not reached rejections 1 and 3–10, although as recognized by Patent Owner, similar rationale would apply.

In addition to the prior art publications, the following declarations have been cited as evidence:

First Declaration by Antonios G. Mikos, Ph.D ("First Mikos Decl.") dated Aug. 27, 2010. Dr. Mikos was a Professor of Bioengineering and Chemical and Biomolecular Engineering in the Departments of Bioengineering and Chemical and Biomolecular Engineering at Rice University at the time the declaration was executed. First Mikos Decl. ¶ 1. Dr. Mikos testified that he has expertise in the synthesis, fabrication and application of biomaterials, specifically polymers, for medical applications, including cardiovascular applications. *Id.* at ¶ 3. Dr. Mikos testified on behalf of the Patent Owner.

2012 Declaration by Michael N. Helmus, Ph.D. ("2012 Helmus Decl.") dated March 30, 2012. Dr. Helmus testified that he is an expert in biomaterials, biocompatibility, and biomaterial databases for medical device applications and currently works as a consult in the field of medical devices. Dr. Helmus testified on behalf of Abbott.

SCOPE AND CONTENT OF THE PRIOR ART[4]

Tuch

Tuch1. Tuch describes an intravascular stent that has a coating on its tissue-contacting surface which comprises a polymer and therapeutic substance. Tuch, col. 2, ll. 36–38.

Tuch2. Tuch teaches that the stent can be of any design, including self-expanding and balloon-expandable types. *Id.* at col. 4, ll. 10–13.

Tuch3. Tuch discloses that the polymer must be biocompatible and minimize irritation to the vessel wall when the stent is implanted. *Id.* at col. 5, ll. 14–16.

Tuch4. Tuch also teaches that the polymer may be either biostable or bioabsorbable. *Id.* at col. 5, ll. 15–16.

Tuch5. Tuch describes "biostable polymers with a relatively low chronic tissue response." *Id.* at col. 5, ll. 33–34.

Tuch6. The list of the biostable polymers includes "vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride [VDF] and polyvinylidene chloride." *Id.* at col. 5, ll. 38–42.

Tuch7. Tuch teaches that during implantation of an expandable stent, the delivery balloon expands and deforms the stent elements and coating. *Id.* at col. 7, ll. 9–11.

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[4] Factual considerations that underlie the obviousness inquiry include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

Tuch8. When the polymeric overlayer on the stent is uniform and "made with materials which have little elasticity," Tuch teaches that "the overlayer can sustain significant cracking during such deformation" and the "cracks can then act as channels for more rapid elution of drugs from the drug-rich base coating." *Id.* at col. 7, ll. 11–15.

Tuch9. Tuch teaches that "cracking of the overlayer can be reduced and drug elution times increased by providing a porous overlayer on the stent." *Id.* at col. 7, ll. 16–18.

Tuch10. Tuch teaches that the coating should be "resilient"[5] for stent expansion: "The inclusion of a polymer in intimate contact with a drug on the stent allows the drug to be retained on the stent in a resilient matrix during expansion of the stent . . ." *Id.* at 2:42–46. In context, Tuch uses the term "resilient" to have its ordinary meaning, which is to be "able to return to an original shape after being pulled, stretched, pressed, bent, etc.," a synonym being "elastic."

Tu

Tu1. Tu describes implantable biomedical devices formed with layers of polytetrafluoroethylene, polytetrafluoroethylene/elastomer, and elastomer. Tu, col 2, ll. 7–37.

Tu2. Tu teaches that its invention relates to various types of implantable bioomedical devices, including heart valve leaflets, and the invention particularly relates to vascular grafts. *Id.* at col. 1, ll. 27–32; col. 2, ll. 36–40.

[5] "Resilient" means "able to return to an original shape after being pulled, stretched, pressed, bent, etc." and a synonym is "elastic." http://www.merriam-webster.com/dictionary/resilient (accessed Jan. 28, 2015).

Tu3. Tu discloses a list of compounds used to prepare the elastomer. *Id.* at col. 2, ll. 20–30. Polyvinylidene fluoride co-hexafluoropropylene (VDF:HFP) is first on the list. *Id.* at col. 2, ll. 23–24.

Tu4. Tu teaches that the elastomer provides elasticity and strength. *Id.* at col. 3, ll. 40–44, 64.

Tu5. According to Tu, the "elastomer solution may optionally contain therapeutic agents including but not limited to antibiotic and/or hemostatic substances." *Id.* at col. 8, ll. 45–47.

Tu6. Tu teaches that the implantable material made of polytetrafluoroethylene and elastomer is biologically compatible. Id. at col. 2, ll. 11–19, 31; col. 3, l.

Lo

Lo1. Lo describes copolymers of vinylidene fluoride (VDF) and hexafluoropropene (HFP) which have flexibility, elasticity, and extensibility. Lo, col. 2, ll. 33–36, 47, and 56–58.

Lo2. Figure 1 of Lo shows an increase of tensile PSIG and reversible elongation from about 86 mol percent to a maximum of about 94 mol percent with a copolymer made of vinylidene fluoride and hexafluropropene.

Lo3. Lo teaches that "[a]bove about 94 mol percent vinylidene fluoride (i.e. less than 6 mol percent hexafluoropropene) the copolymer is essentially crystalline in nature and the reversible elongation decreases rapidly." Lo, col. 9, ll. 33–36.

Lo4. The Examiner found that "copolymers with an optimal combination of tensile strength and reverse elongation are achieved at 93 mol % VDF, corresponding to a VDF/HFP wt% ratio of 85:15 (Fig. 1; col. 9, lines 15–27)."

RAN 14. Dr. Mikos in his declaration acknowledged that "Lo describes VDF/HFP coatings having VDF:HFP weight percent of 85: 15." First Mikos Decl. ¶ 41.

Le Morel[6]

LeM1. LeMorel teaches implants such as stents. LeMorel 2:4–15.

LeM2. Le Morel teaches that the substrate of the implant can be a polymer, and specifically identifies copolymers of vinylidene fluoride and hexafluorpropylene among a list. *Id.* at 3:1–5 and 18–19.

LeM3. Le Morel teaches in the case of stents, a fluorinated polymer is advantageous. *Id.* at 4:4–10.

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE PRIOR ART

The Examiner found that Tuch describes a balloon-expandable stent having a coating containing a therapeutic agent, meeting the claimed limitation of "a balloon-expandable stent and a pharmaceutical agent-containing coating." RAN 13-14; Tuch1–2, 7. The Examiner found that the coating may be formed with VDF. RAN 14; Tuch6. The Examiner found that Tuch does not describe a coating "that comprises about eighty-five weight percent vinylidinefluoride [VDF] copolymerized with about fifteen weight percent hexafluoropropylene [HFP]," but found that Lo describes such a copolymer coating and its advantages with respect tensile strength and reversible elongation. RAN 14; Lo1–4. Furthermore, the

[6] Le Morel et al. (Le Morel or LeM) FR 2,785,812 Nov. 16, 1998. Citations to translation of record.

Examiner found that Tu demonstrates the biocompatibility of VDF/HFP polymers and that such copolymers can contain therapeutic substances. RAN 14; Tu5.

Based on the teachings of Lo and Tu, the Examiner determined it would have been obvious to one of ordinary skill in the art to have replaced "Tuch's crystalline VDF homopolymer with the partially crystalline copolymers having a VDF/HFP wt % ratio of about 85:15 (as recited in [device] claim 1 and method claim 19) . . . to arrive [at] the instant invention." RAN 14–15. The Examiner's rationale was that a person of ordinary skill in the art would have understood that VDF/HFP is advantageous as compared to VDF homopolymers and has optimal tensile strength and reversible elongation at VDF/HFP wt% ratio of 85:15 as shown by Lo. *Id.* at 14.

Discussion

Patent Owner contends that the Examiner erred in combining the publications to have arrived at the claimed invention. Specifically, Patent Owner argues that one of ordinary skill in the art reading Tuch would not have had reason to choose polymers from publications other than Tuch because Tuch did not identify a problem with its polymers used for its drug coating layer. Appeal Br. 16. Patent Owner also argues that it is improper to combine Tu's teachings with those of Tuch. *Id.* at 17.

Choice of VDF:HFP

It is unnecessary that Tuch disclose any shortcomings in its list of polymers for the ordinary skilled worker to have found it obvious to have employed an alternative polymer for its coating since it is obvious to use a prior art element for

its established function. As held in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007), in making an obviousness determination, it must be asked "whether the improvement is more than the predictable use of prior art elements according to their established functions." Thus, even if Tuch did not disclose a problem with its polymers, one of ordinary skill in the art would have found it obvious to have employed the known polymers of Tu and Lo for their known and expected properties. As argued by Abbott, Abbott Respondent Br. 12, the reason to combine could be provided by the "normal desire of scientists or artisans to improve upon what is already generally known." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003).

In addition to this, Tuch does not limit its polymers to those specifically disclosed. Tuch teaches using "vinyl halide polymers and copolymers," and specifically discloses "polyvinylidene halides, such as polyvinylidene fluoride." Tuch6. This disclosure, while mentioning a specific polyvinylidene halide, also includes broader classes ("vinyl halides" and "polyvinylidene halides"), including copolymers, which would have reasonably suggested that additional polymers, outside those specifically described in Tuch, would be useful as Tuch's polymer coating comprising a therapeutic substance.

To support their position about the unobviousness of using polymers other than those disclosed in Tuch, Patent Owner cites *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342,1370–71 (Fed. Cir. 2012).

> As in *Kinetic Concepts, Inc.* 688 F.3d at 1369, a case in which the Federal Circuit overturned a prior finding of obviousness, the record here "is devoid of any reason someone would combine [the cited] references." Where, as here, each device that the references describe "independently operates effectively," a person having ordinary skill in

> the art "would have no reason" to combine the reference" respective teachings. *Id.*

Appeal Br. 17. *See* also Rebuttal Br. 3.

In *Kinetic*, the issue was whether to combine publications which "both . . . independently accomplish similar functions, namely, draining fluids." *Kinetic Concepts, Inc.* 688 F.3d at 1369. One set of publications involved negative pressure to drain wounds. *Id.* at 1362-1363. The other set of publications disclosed a different type of wound drainage system. *Id.* at 1365. The obviousness rejection was predicated on combining the two sets of publications to meet a limitation in the claim of using negative pressure to treat a wound, where wound treatment had not been found to be present in the negative pressure publications. *Id.* at 1361, 1363. Because each publication was complete in teaching a wound drainage method, and there was no teaching that negative pressure could be used to treat wounds, the court found "a person having ordinary skill in the art, who was merely seeking to create a better device to drain fluids from a wound, would have no reason to combine the features of both devices into a single device." *Id.* at 1369.

The facts of this case are clearly distinguishable. Tuch teaches various polymer coatings for its stent, including broad classes that encompass unnamed species. Tu was cited in the rejection for teaching polymers suitable for Tuch's stent coating. The reason to consult Tu is because Tuch's list of polymers is clearly not exhaustive in view of Tuch's description of broad classes of polymers, such as vinyl halide polymers and copolymers, and polyvinylidene halides. Tuch6. Tuch also uses the transitional phrase "such as" in prefacing the list of biostable polymers and in reciting specific examples of the broader classes, indicating that Tuch did not confine the skilled worker to the explicit list, but contemplated

polymers outside of it. ("Also, biostable polymers with a relatively low chronic tissue response such as . . . and other polymers could also be used if they can be dissolved and cured or polymerized on the stent such as . . . vinyl halide polymers and copolymers, such as . . . " Tuch, col. 5, ll. 33–39).

Patent Owner argues that Tuch recites a long laundry list of polymers and therefore would not have directed the skilled worker to the specifically claimed polymers. Appeal Br. 24. First Mikos Decl. ¶¶ 52–56.

The fact that "vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride [VDF] and polyvinylidene chloride" appear in a longer list (Tuch6) would not have dissuaded one of ordinary skill from choosing VDF copolymers. The list recited in Tuch is of polymers that Tuch considered useful for its stent coating and therefore is a disclosure of each and every one for a stent coating. There does not have to be a working example of vinyl halide polymer copolymer, polyvinylidene halide, or VDF, as alleged by Dr. Mikos (First Mikos Decl. ¶ 143) for one of ordinary skill in the art to have recognized such compounds as useful for a polymer coating since Tuch expressly describes their use for this purpose. Tuch6.

Furthermore, Patent Owner admitted in the "Background" of the '844 patent that "[s]tents with coatings made from polyvinylidenefluoride homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested." '844 patent, col. 5, ll. 4–6. *See* also "Preexamination Search Statement and Accelerated Examination Support Document" 12 ("AESD"; filed Nov. 16, 2007 in the application that led to the '844 patent) identifying the latter statement as prior art.

Dr. Mikos attempts to distinguish Tuch because Tuch describe a porous overlayer of polymer to control drug release. First Mikos Decl. ¶ 144. However, the claim does not exclude such a porous layer made of VDF:HFP.

Patent Owner also argues that the stent coating in Tuch is in contact with the vessel wall lining and in contact with blood, while in Tu, the graft's inner surface which contacts the blood lacks the elastomer. Appeal Br. 23. While this might be the case, Tu teaches that it's the polytetrafluoroethylene/elastomer which can be used generally in other medical devices, such as a heart valve leaflet that could be in contact with blood. Tu2.

Is there an adequate reason to have combined Tuch and Tu?

Patent Owner argues that the record is devoid of reason to have combined Tuch and Tu. Appeal Br. 17. Patent Owner also argues that Tu relates to vascular grafts and therefore is not relevant to Tuch.[7] *Id.* at 18:1–2.

A preponderance of the evidence does not support Patent Owner's position that the record lacks a reason to combine Tuch with Tu.

First, Tu is not limited to vascular grafts, but clearly teaches that its polymers are useful for various types of implantable devices. Tu2. While vascular grafts are preferred, such preference does not negate the broader teaching.

Second, Tu's polyvinylidene fluoride co-hexafluoropropylene has the properties described in Tuch as useful for its stent coating. These properties are discussed below:

1) Tuch's polymers are biocompatible as they are in Tu. Tuch3; Tu6.

[7] Taking a contrary position, in the AESD filed in the application that led to the '844 patent, Patent Owner characterized Tu (US 5,061,276) as one of the "most closely related" prior art references. AESD 6. Abbott Respondent Br. 15.

2) Tuch teaches elastic polymers are beneficial for coatings in expandable stents. Tuch8, 10. Tu's elastomers are elastic. Tu4.

Patent Owner contends that elasticity would not have been a factor in choosing a polymer coating for Tuch's stent. Appeal Br. 18–19. However, Tuch teaches that, when the stent delivery balloon expands, the stent coating can deform. Tuch7. When materials are used for the polymers which "have little elasticity," the polymer overlayer can crack during the expansion and result in rapid drug elution. Tuch8. Tuch teaches one way to reduce the cracking. Tuch9. Since Tuch teaches a problem with cracking when materials having little elasticity are utilized in the polymer layer, one of ordinary skill in the art would have reasonably sought materials with high elasticity to avoid the problem when the stent is expanded.

Furthermore, Tuch teaches that using a resilient matrix during expansion of the stent is beneficial for drug retention. Tuch10. Resilient is a synonym for elastic. Fn. 5. *See* also 2012 Helmus Decl. ¶ 6 for further evidence of the desirability of an elastic polymer. Tu teaches elastomers that provide elasticity and strength. Tu4.

Dr. Mikos testified that the "physical and mechanical properties that are important for the Tu vascular grafts . . . are very different from the physical and mechanical properties that are important for polymer coatings used on balloon expandable stents [as in Tuch]." First Mikos Decl. ¶ 43. Dr. Mikos identifies elasticity as important in vascular grafts. *Id.* at ¶ 44. Dr. Mikos, however, did not explain how elasticity is distinguishable from the ability of a polymer to be elongated or deformed before breaking which he identified as an "important property" of a stent polymer coating. *Id.* at ¶¶ 46, 147. That is, while Tu's graft may have a different purpose than Tuch's stent, Dr. Mikos admits that a stent

coating must be resilient (resist deformation before breaking) which is the same property that Dr, Mikos identifies as important in vascular grafts. Consequently, Dr. Mikos's testimony about the lack of reason to combine Tuch and Tu is not supported by persuasive factual evidence.

3) Tuch teaches that polyvinylidene fluoride is a useful polymer for its coating comprising a therapeutic substance. Tuch1, 6. The first elastomer on Tu's list is a copolymer comprising polyvinylidene fluoride and hexafluoropropylene (VDF:HFP). Tu3. The obviousness of choosing VDF:HFP as a stent coating is further evidenced by Le Morel who describes the copolymer as coating on a stent. LeM1–3.

4) Tuch teaches a polymer coating that delivers a therapeutic substance. Tuch1. Tu also teaches that its elastomer can contain therapeutic agents. Tu5.

Summary

In sum, a preponderance of the evidence supports the determination it would have been obvious to have selected VDF:HFP from Tu as the polymer coating in Tuch. Contrary to Patent Owner's statement that it would have been a scavenger hunt to find VDF:HFP (Hearing Tr. 4:6–11), VDF:HFP is disclosed by Tu as a useful elastomer for an implantable medical device and Tu's elastomers have the properties described by Tuch as advantageous in a stent, which is an example of an implantable device.

Proportion of VDF and HFP

As far as the 85:15 copolymer of VDF and HFP recited in the claims, Lo teaches that a 85:15 copolymer is advantageous with respect to flexibility,

elasticity, extensibility, tensile strength, and reverse elongation. Lo1–4; RAN 14. One of ordinary skill in the art would have been motivated to have used Lo's polymer having these advantageous properties as the coating in Tuch because Tuch teaches a problem with coatings with low elasticity (Tuch8-9).

Because VDF:HFP is expressly described by Tu as useful for an implantable medical device (Tu2), the skilled worker would have reasonably consulted Lo to determine the optimal concentrations for each component, even if Lo does not teach the use of VDF:HFP for medical implants. Patent Owner's argument that Lo's uses are industrial and therefore not pertinent to stents (Appeal Br. 24; First Mikos Decl. ¶¶ 41–42) is unavailing since Lo was cited for teaching the properties of VDF:HFP which had been taught to be useful by Tu in a medical device.

Patent Owner's argument that VDF:HFP is not described as a carrier for a drug has little merit. Appeal Br. 25. As mentioned, Tu teaches that its elastomer may contain therapeutic agents. Tu5.

SECONDARY CONSIDERATIONS

Factual considerations that underlie the obviousness inquiry include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations. *Graham.*, 383 U.S. at 17-18. Relevant secondary considerations include commercial success, long-felt but unsolved needs, failure of others, praise, and unexpected results. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007); *Institut Pasteur & Universite Pierre et Marie Curie v. Focarino*, 738 F.3d 1337, 1344 (Fed. Cir. 2013); *In re Soni*, 54 F.3d 746 (Fed. Cir. 1995). Secondary considerations are "not just a cumulative or confirmatory part of the obviousness

calculus but constitute [] independent evidence of nonobviousness . . . [and] enable [] the court to avert the trap of hindsight." *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013) (internal quotation marks and citations omitted). "This objective evidence must be 'considered as part of all the evidence, not just when the decisionmaker remains in doubt after reviewing the art.'" *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012) (internal citations omitted).

Patent Owner contends that the Examiner failed to credit the evidence of nonobviousness of the claimed invention. Appeal Br. 9–10. As evidence, Patent Owner cited studies performed with the Xience V stent. Patent Owner asserts that Xience V is a stent sold by Abbott Laboratories that "employs Solef® 21508 (Patent Owner's Response to ACP, at pg. 16), a VDF:HFP copolymer that comprises about 85% VDF and about 15% HFP." Appeal Br. 11.

Copying

Patent Owner states that the invention of the '844 Patent has been copied and adopted by others in the industry, including by Abbott (Xience V stent) and by Boston Scientific (Promus stent). Appeal Br. 9–10. As evidence, Patent Owner cites to paragraph 224 of the first Mikos declaration. However, paragraph 224 merely alleges copying by Abbott and Boston Scientific without factual evidence or analysis to support this statement. RAN 71. Consequently, without adequate evidence that Abbott and Boston Scientific copied the claimed invention, we give this argument little weight.

Commercial success

Patent Owner contends that commercial success of the claimed invention is demonstrated by the statement in Abbott's 2008 Form 10K that "'Xience V became the market-leading drug eluting stent in the U.S. in the fourth quarter of 2008,' within just three months of FDA approval" and Dr. Mikos's statement that the "PVDF-HFP coating used in the Xience V stent is an important factor in the clinical success of the Xience V stent, and therefore also in the commercial success of the Xience V and Promus stents. First Mikos Decl. ¶ 227. Patent Owner further cited Abbott's fact sheet on the Xience V stent which represented that "the composition of the polymer coating" in the Xience V stent "is important in overall clinical safety and efficacy outcomes." Appeal Br. 11 (fn. 4). Patent Owner also cited evidence that Xience's thin, nonreactive polymer accounted for its success. *Id.* at 12 (fn. 5).

For evidence of secondary considerations to be accorded substantial weight, there must be a nexus between the claimed invention and what is relied upon as the secondary consideration. *In re GPAC*, Inc., 57 F.3d 1573, 1580 (Fed. Cir. 1995). A nexus is established when the secondary consideration is attributed to a feature of the claimed invention. *Ormco Corp. v. Align Tech.*, Inc., 463 F.3d 1299, 1311–12.

In this case, even if there is evidence that the coating is one factor that contributed to the success of Xience, there is additional evidence that the drug and stent material are also important reasons for its success. Neither the drug nor the stent material is recited in claims 1 and 19. In this regard, as noted by the Examiner (RAN 73), Ex. 10 describes the drug and stent frame as reasons for the success of Xience V:

> Assessing why second-generation DES such as Xience may be superior to earlier-generation stents, the editorialists point out that they may differ on many fronts: the antiproliferative agent (in this case everolimus vs. paclitaxel), the polymer layer (Xience's is biocompatible), and stent frame (flexible cobalt-chromium vs. stainless steel). For example, improved stent design may result in better stent apposition and endothelialization as well as reduced platelet aggregation and thrombus formation. However, since the relative contribution of each of these elements to the enhanced performance of Xience is unknown, the study results are not necessarily applicable to other everolimus-eluting stents, Drs. Lange and Hillis caution.

Ex. 10

Similarly, Exhibit 9 states:

> Everolimus is a more potent drug than those used in the first-generation coated stents and also is contained in a thin, inert polymer that is less likely to cause inflammation, Stone said. The Xience stent itself is also thinner than the previous devices, he added.

Patent Owner represented that Dr. Stone had attributed Xience's commercial success to the polymer coating. Appeal Br. 12 (fn. 5). However, in theheart.org it was reported that Dr. Stone highlighted several reasons for the success of Xience, and not only the polymer coating as indicated by Patent Owner:

> Stone, who first presented the SPIRIT III results at the TCT 2007 meeting, told heartwire that two-year results will be presented at the upcoming EuroPCR meeting in Barcelona. He highlighted design characteristics of the Xience—**thinner struts; a thin, nonreactive polymer; and a drug with similar potency to sirolimus**—as key reasons not only for the reduced late loss at nine months, fewer repeat procedures at one year, and fewer procedural MIs, but also as factors that may ensure the stent also performs better over time.

theheart.org (emphasis added).

Thus, it has not been established that the claimed polymer in the 85:15 wt% ratio is responsible for the asserted success of the claimed invention, rather than

the drug or the stent material—both which are unclaimed features. Accordingly, the preponderance of the evidence does not support a nexus between commercial success and the merits of the claimed invention ("For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *GPAC*, 57 F.3d at 1580).

Unexpected results

A showing of "unexpected results" can be used to demonstrate the non-obviousness of the claimed invention. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("One way for a patent applicant to rebut a *prima facie* case of obviousness is to make a showing of 'unexpected results,' *i.e.*, to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected."). Those results must be "surprising or unexpected" to one of ordinary skill in the art when considered in the context of the closest prior art. *Soni*, 54 F.3d at 750; *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004) (A showing of "new and unexpected results" must be "relative to prior art."); *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) ("[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art"). To establish unexpected results, the claimed subject matter must be compared with the closest prior art. *Baxter*, 952 F.2d at 392.

Citing paragraph 25 of Dr. Mikos's first declaration, Patent Owner contends that "the PVDF-HFP coated Xience V stent is more thromboresistant (*i.e.*, shows greater tendency to reduce thrombus formation) than other drug-eluting stent

coatings." Appeal Br. 12. Patent Owner also contends that "numerous clinicians have also emphasized that the PVDF-HFP polymer used in the Xience V stent shows unexpectedly less inflammation," again citing to the Mikos declaration. *Id.*

Paragraph 227 of the Mikos declaration refers to Abbott's data in Exhibits 7 and 8. Exhibit 7 is undated. Exhibit 7 at ABT046618 shows that the weight of thrombus adhered to the stent for Xience V was less than for the Cypher, Endeavor, and Taxus Liberté stents. ABT046619 shows that Xience V had lower thrombus adherence "due to smooth coating integrity and hemocompatability of the XIENCE V Fluoropolymer" as compared to the Vision stent.

Dr. Mikos did not fully describe the coatings, stent materials, or therapeutic agents utilized in the stents to which the performance of Xience V was compared. Cypher comprises the drug sirolimus combined with a polymer blend of two non-erodible polymers, polyethylene-co-vinyl acetate (PEVA) and poly n-butyl methacrylate (PBMA), to form the basecoat. First Mikos Decl. ¶ 24. To establish unexpected results, the comparison must be against the closest prior art. *Baxter*, 952 F.2d at 392; *Iron Grip Barbell Co.*, 392 F.3d at 1322. Dr. Mikos did not establish that the coating on Cypher constitutes the closest prior art.

In addition to this, Dr. Mikos did not provide evidence that the purported improved results for Xience V was due to a claimed feature, rather than an unclaimed feature, such as the drug or stent material. *Ormco Corp,* 463 F.3d at 1311–12. Dr. Mikos also did not state the results would have been unexpected or surprising to one of ordinary skill in the art. *Soni*, 54 F.3d at 750.

Exhibit 8 was also cited by Dr. Mikos as evidence of unexpected results. Exhibit 8 is undated. Dr. Mikos cited page 28 of Exhibit 8. This page shoes that the average thrombus weight for Xience was less than for "Vision BMS." "BMS"

is a bare metal stent. Ex. 8, p. 28. The comparison therefore does not appear to be with the closest prior art since Tuch describes coated stents and Vision BMS is bare metal. Tuch1, Tuch3–6. *Baxter*, 952 F.2d at 392.

Dr. Mikos further testified in his written declaration that "numerous clinicians have also emphasized that the PVDF-HFP polymer used in the Xience V stent shows unexpectedly less inflammation." First Mikos Decl. ¶ 228. As evidence, Dr. Mikos cited Exhibits 9 and 10.

Exhibit 9 is a news article. The article mentions that Xience V is "less likely to cause inflammation." Exhibit 10 is also a news article. The article states:

> In a telephone interview with TCTMD, Robert S. Schwartz, MD, of the Minneapolis Heart Institute Foundation (Minneapolis, MN), underlined the role of the polymer in differentiating between the stent generations, saying that Taxus' older polymer was more likely to induce inflammation.

This evidence is not persuasive since it does not establish that the reduction in inflammation observed with Xience V is in comparison with the closest prior art as required under *Baxter*, 952 F.2d at 392. Rather, it appears the news articles are reporting that Xience's polymer is less inflammatory than the polymers on existing stents. Patent Owner has not provided sufficient testimony that this reduced inflammation would have been unexpected by one of ordinary skill in the art in comparison to the polymers described in Tuch, for example, which teaches stents with polymer coatings, including a homopolymer of VDF (Tuch6).

Consequently, the evidence does not support Dr. Mikos's opinion in paragraph 228 about unexpected results associated with the claimed polymer.

Industry praise

Patent Owner states that there "has been industry praise for Xience V that is attributable to the claimed invention." Appeal Br. 11.

We have reviewed Exhibits 6, 9, and 10, each of which describes success with Xience. However, as discussed above, it is not evident from these articles that the success and praise is a result of the claimed invention, rather than and unclaimed feature such as the drug or stent design. Exhibit 10, for example, compares Xience containing the everolimus drug in its coating with a paclitaxel stent. The article asks "'Should we abandon paclitaxel-eluting stents in favor of second-generation everolimus-eluting stents on the basis of the results of [this] study'," indicating that, at least in this case, the praise and success may be related to the everolimus drug.

SUMMARY

After considering the evidence in this record, including the evidence of secondary considerations and the declarations, we conclude that a preponderance of the evidence supports the Examiner's determination that claims 1 and 19 are unpatentable under 35 U.S.C. § 103(a) (pre-AIA) as obvious in view of Tuch, Tu, and Lo. Dependent claims 2–17 and 20–23 were not argued separately. We affirm the rejection of these claims for the reasons given by the Examiner.

TIME PERIOD FOR RESPONSE

In accordance with 37 C.F.R. § 41.79(a)(1), the "[p]arties to the appeal may file a request for rehearing of the decision within one month of the date of: . . . [t]he original decision of the Board under § 41.77(a)." A request for rehearing must be in compliance with 37 C.F.R. § 41.79(b). Comments in opposition to the

request and additional requests for rehearing must be in accordance with 37 C.F.R. § 41.79(c) & (d), respectively. Under 37 C.F.R. § 41.79(e), the times for requesting rehearing under paragraph (a) of this section, for requesting further rehearing under paragraph (d) of this section, and for submitting comments under paragraph (c) of this section may not be extended.

An appeal to the United States Court of Appeals for the Federal Circuit under 35 U.S.C. §§ 141–144 and 315 and 37 C.F.R. § 1.983 for an *inter partes* reexamination proceeding "commenced" on or after November 2, 2002 may not be taken "until all parties' rights to request rehearing have been exhausted, at which time the decision of the Board is final and appealable by any party to the appeal to the Board." 37 C.F.R. § 41.81. *See also* MPEP § 2682 (8th ed., Rev. 7, July 2008).

In the event neither party files a request for rehearing within the time provided in 37 C.F.R. § 41.79, and this decision becomes final and appealable under 37 C.F.R. § 41.81, a party seeking judicial review must timely serve notice on the Director of the United States Patent and Trademark Office. See 37 C.F.R. §§ 90.1 and 1.983.

AFFIRMED

Appeal 2014-008135
Reexamination Control 95/000,542 and 95/000,552
Patent 7,591,844 B2

PATENT OWNER:

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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.
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lb

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/000,542	04/15/2010	7,591,844 B2	CRDS-0116	8264

45511 7590 04/14/2015

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EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
04/14/2015	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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MAIL DATE	DELIVERY MODE
04/14/2015	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE
PATENT TRIAL AND APPEAL BOARD

BOSTON SCIENTIFIC SCIMED, INCORPORATED
and ABBOTT LABORATORIES,
Requesters #1 & 2

v.

CORDIS CORPORATION and WYETH
Patent Owners

Appeal No. 2014-008135
Merged Reexamination 95/000,542 & 95/000,552
Patent 7,591,844
Technology Center 3900

DECISION ON PETITIONS

Patent Owner, Cordis Corporation, requests permission to cross-examine adverse expert witnesses whose declaration testimony has been entered into the record of merged *Inter Partes* Reexaminations 95/000,542 & 95/000,552. (Petition). This is a decision dismissing "PATENT OWNER'S PETITION FOR THE CHIEF ADMINISTRATIVE PATENT JUDGE'S EXERCISE OF STATUTORY AUTHORITY," filed on January 15, 2015; dismissing "REQUESTER'S OPPOSITION TO PATENT OWNER'S PETITION FOR THE CHIEF ADMINISTRATIVE PATENT JUDGE'S EXERCISE OF PURPORTED STATUTORY AUTHORITY," filed on January 20, 2015, (Opposition); and

dismissing "REQUESTER ABBOTT'S PETITION TO RESPOND TO PATENT OWNER CORDIS'S JANUARY 15, 2015 PETITIONS FOR THE CHIEF ADMINISTRATIVE PATENT JUDGE'S EXERCISE OF STATUTORY AUTHORITY," filed on January 22, 2015 (3PR petition). The petition fee of $1,940 in accordance with 37 C.F.R. § 1.20(c)(6) was charged to Patent Owner's deposit account on January 16, 2015. The petition fees of $400 were charged to Requester's credit card on January 20, 2015, and January 23, 2015, respectively.

FINDINGS

1. On June 12, 2013, Patent Owner filed a petition entitled "PATENT OWNER'S SUPPLEMENTAL SUBMISSION IN SUPPORT OF PETITION FOR DIRECTOR'S EXERCISE OF STATUTORY AUTHORITY."

2. The appeal was docketed at the Board on August 5, 2014.

3. On December 4, 2014, a "Decision Denying Petition" was mailed by the Commissioner for Patents, denying the Patent Owner's petition of June 12, 2013.

4. Patent Owner filed the present petition on January 15, 2015.

5. Requester, Abbott Laboratories, filed an opposition to the petition on January 20, 2014, and a petition for authorization to file an opposition on January 22, 2015.

6. A Decision on the appeal was rendered on February 27, 2015, affirming the Examiner's rejections of the claims.

DISCUSSION

In the present petition, Patent Owner requests permission to cross-examine adverse expert witnesses whose declaration testimony has been entered into the record of merged *Inter Partes* Reexaminations 95/000,542 & 95/000,552. In its opposition, Requester, Abbott Laboratories opposes the petition, and appears to seek authorization to oppose the petition, after the filing of the opposition.

RELEVANT AUTHORITY

35 U.S.C. § 314(c) (pre-AIA) provides:

> SPECIAL DISPATCH.— Unless otherwise provided by the Director for good cause, all inter partes reexamination proceedings under this section, including any appeal to the Patent Trial and Appeal Board, shall be conducted with special dispatch within the Office.

37 C.F.R. § 41.3 provides:

> (a) Deciding official. Petitions must be addressed to the Chief Administrative Patent Judge. A panel or an administrative patent judge may certify a question of policy to the Chief Administrative Patent Judge for decision. The Chief Administrative Patent Judge may delegate authority to decide petitions.
>
> (b) Scope. This section covers petitions on matters pending before the Board (§§ 41.35, 41.64, 41.103, and 41.205); otherwise, see §§ 1.181 to1.183 of this title. The following matters are not subject to petition:
>
> > (1) Issues committed by statute to a panel, and
> >
> > (2) In pending contested cases, procedural issues. See § 41.121(a)(3) and § 41.125(c).
>
> (c) Petition fee. The fee set in § 41.20(a) must accompany any petition under this section except no fee is required for a petition under this section seeking supervisory review.

> (d) Effect on proceeding. The filing of a petition does not stay the time for any other action in a Board proceeding.
>
> (e) Time for action.
>
> > (1) Except as otherwise provided in this part or as the Board may authorize in writing, a party may:
> >
> > > (i) File the petition within 14 days from the date of the action from which the party is requesting relief, and
> > >
> > > (ii) File any request for reconsideration of a petition decision within 14 days of the decision on petition or such other time as the Board may set.
> >
> > (2) A party may not file an opposition or a reply to a petition without Board authorization.

37 C.F.R. § 1.939(a) provides:

> If an unauthorized paper is filed by any party at any time during the inter partes reexamination proceeding it will not be considered and may be returned.

ANALYSIS

In the present petition, Patent Owner requests permission to cross-examine adverse expert witnesses whose declaration testimony has been entered into the record of merged *Inter Partes* Reexaminations 95/000,542 & 95/000,552. Petition 1. In a "Decision Denying Petition" mailed on December 4, 2014, the Commissioner for Patents issued a decision on this matter, which concluded with the statement, "[t]his decision constitutes the Office's final decision on these issues." Petition 4. Because Patent Owner already has received a final agency decision on this matter, the present petition is **dismissed** as an improper submission, will not be

considered, and will be closed from the Image File Wrapper (IFW) system. With regard to the opposition, Requester did not seek authorization pursuant to 37 C.F.R. § 41.3(e)(2), prior to filing the opposition. Therefore, the opposition is **dismissed** as an unauthorized submission, and will be closed from the Image File Wrapper (IFW) system.

CONCLUSION

Patent Owner's Petition is DISMISSED; Requester's Opposition and Petition requesting authorization to file the opposition are DISMISSED; and all three documents will be closed from the IFW system.

James Donald Smith
Chief Administrative Patent Judge

Appeal No. 2014-008135
Merged Reexamination 95/000,542 & 95/000,552
Patent 7,591,844

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WASHINGTON, DC 20001-4413


US007591844B2

(12) **United States Patent**
Llanos et al.

(10) **Patent No.: US 7,591,844 B2**
(45) **Date of Patent: *Sep. 22, 2009**

(54) **MEDICAL DEVICES, DRUG COATINGS AND METHODS FOR MAINTAINING THE DRUG COATINGS THEREON**

(75) Inventors: **Gerard H. Llanos**, Stewartsville, NJ (US); **Mark B. Roller**, North Brunswick, NJ (US); **Angelo George Scopelianos**, White House Station, NJ (US); **Robert Falotico**, Belle Mead, NJ (US)

(73) Assignees: **Cordis Corporation**, Miami Lakes, FL (US); **Wyeth**, Madison, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **11/941,351**

(22) Filed: **Nov. 16, 2007**

(65) **Prior Publication Data**

US 2008/0051865 A1 Feb. 28, 2008

Related U.S. Application Data

(63) Continuation of application No. 11/782,770, filed on Jul. 25, 2007, now abandoned, which is a continuation of application No. 11/437,572, filed on May 19, 2006, which is a continuation of application No. 10/636,435, filed on Aug. 7, 2003, now Pat. No. 7,056,550, which is a continuation of application No. 09/962,496, filed on Sep. 25, 2001, now abandoned, which is a continuation-in-part of application No. 09/675,882, filed on Sep. 29, 2000, now abandoned.

(51) **Int. Cl.**
A61F 2/06 (2006.01)
B32B 27/00 (2006.01)
A61L 33/00 (2006.01)

(52) **U.S. Cl.** **623/1.12**; 623/1.43; 623/1.46; 623/1.49; 428/421; 427/2.25

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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Ullmann's Encyclopedia of Industrial Chemistry, Wolfgang Gerhartz et al. (eds.), 5th completely rev. ed., vol. A11, VCH Publishers, p. 417, 1988.

* cited by examiner

Primary Examiner—Robert M Kelly
(74) *Attorney, Agent, or Firm*—Woodcock Washburn LLP

(57) **ABSTRACT**

Medical devices, and in particular implantable medical devices, may be coated to minimize or substantially eliminate a biological organism's reaction to the introduction of the medical device to the organism. The medical devices may be coated with any number of biocompatible materials. Therapeutic drugs, agents or compounds may be mixed with the biocompatible materials and affixed to at least a portion of the medical device. These therapeutic drugs, agents or compounds may also further reduce a biological organism's reaction to the introduction of the medical device to the organism. Various materials and coating methodologies may be utilized to maintain the drugs, agents or compounds on the medical device until delivered and positioned.

24 Claims, 19 Drawing Sheets

FIG. 1

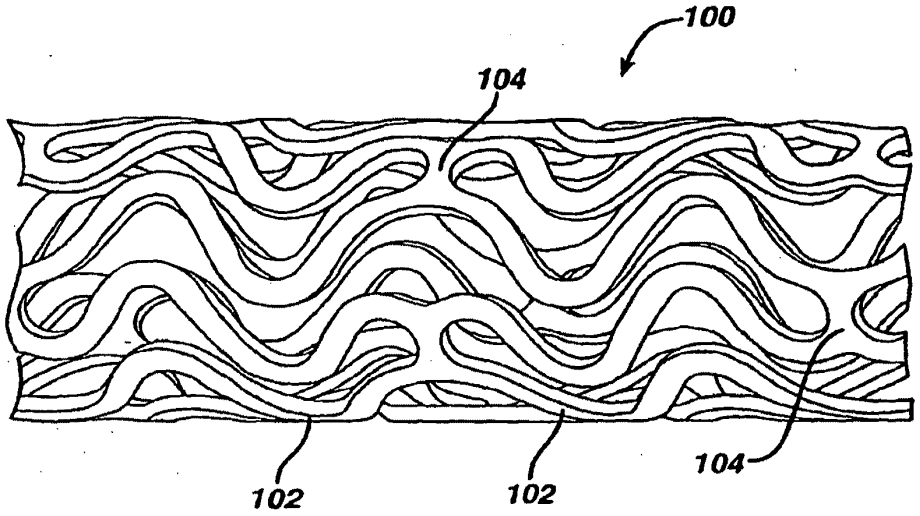


FIG. 2

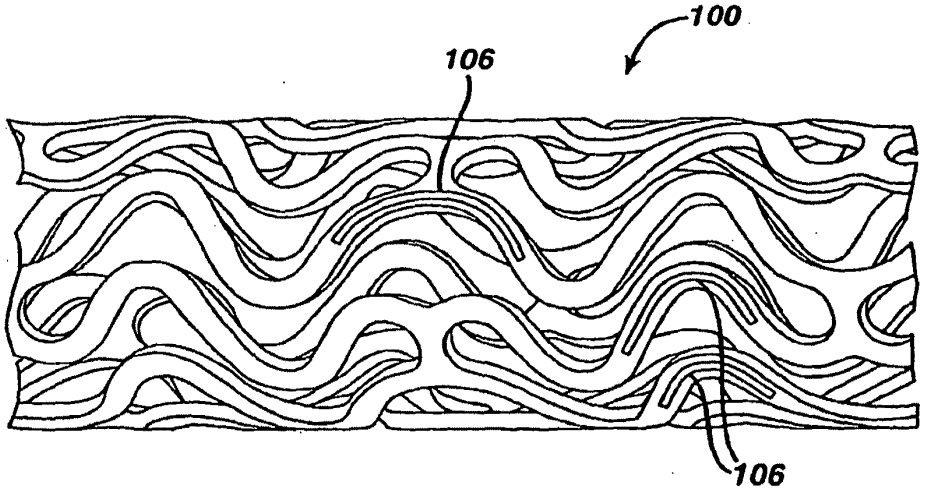


FIG. 3

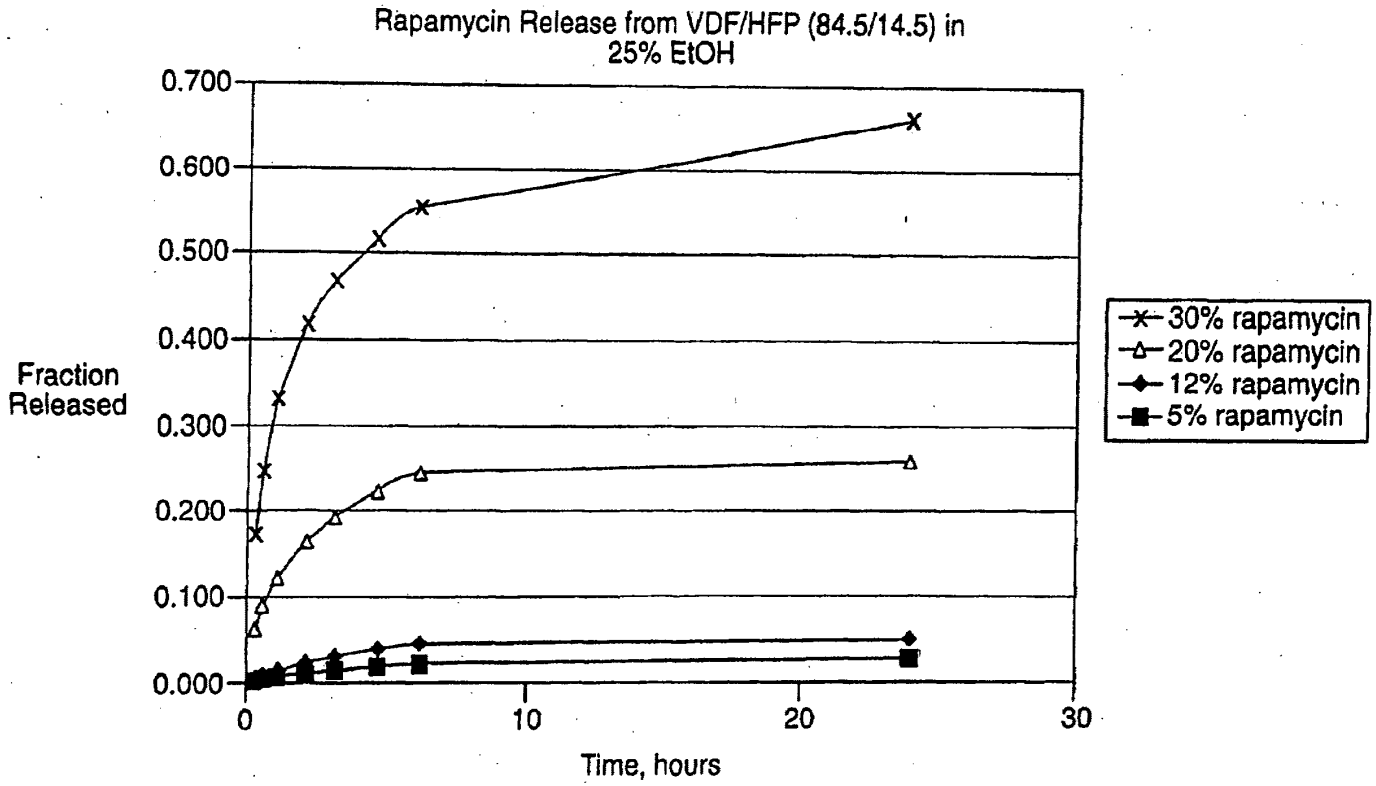

Rapamycin Release from VDF/HFP (84.5/14.5) in 25% EtOH
Fraction Released
0.700
0.600
0.500
0.400
0.300
0.200
0.100
0.000
0
10
20
30
Time, hours
30% rapamycin
20% rapamycin
12% rapamycin
5% rapamycin

FIG. 4

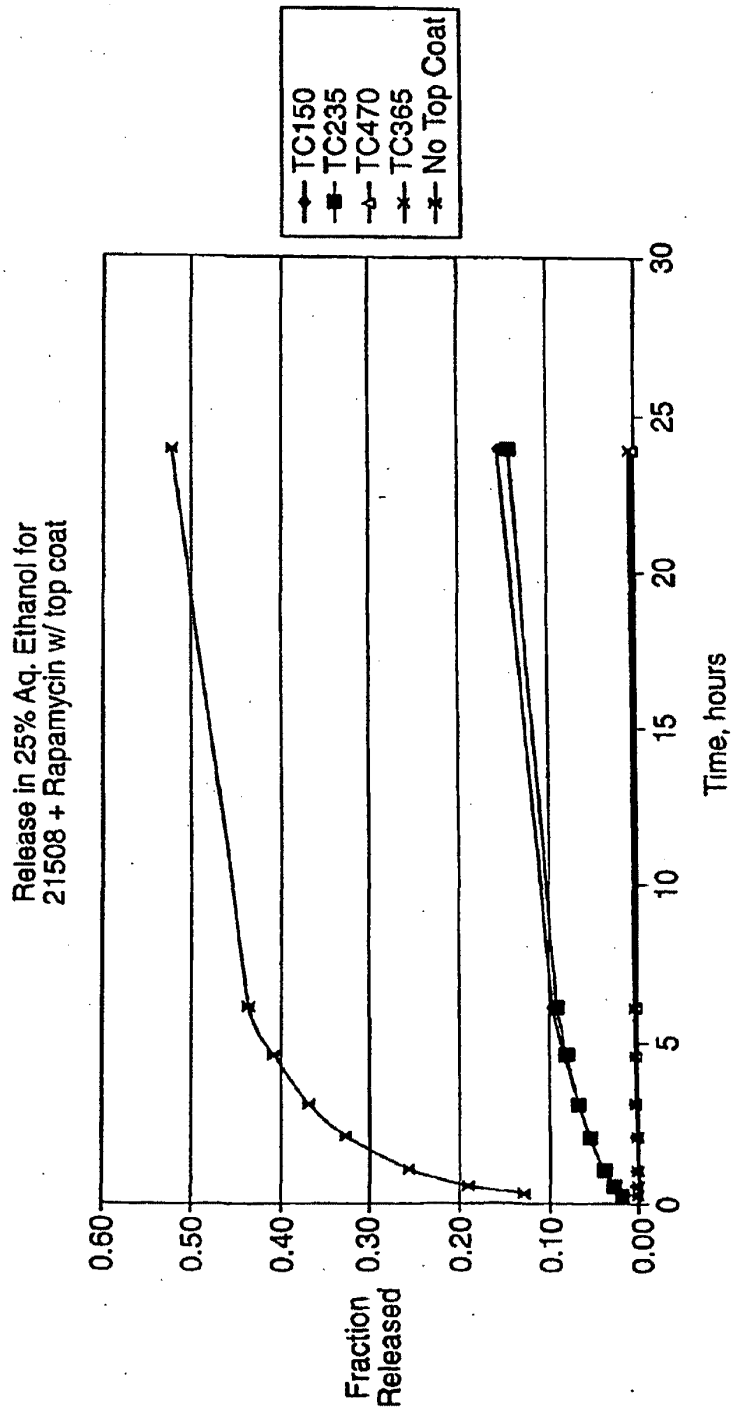

TC150
TC235
TC470
TC365
No Top Coat
Release in 25% Aq. Ethanol for 21508 + Rapamycin w/ top coat
Fraction Released
0.60
0.50
0.40
0.30
0.20
0.10
0.00
Time, hours
0
5
10
15
20
25
30

FIG. 5

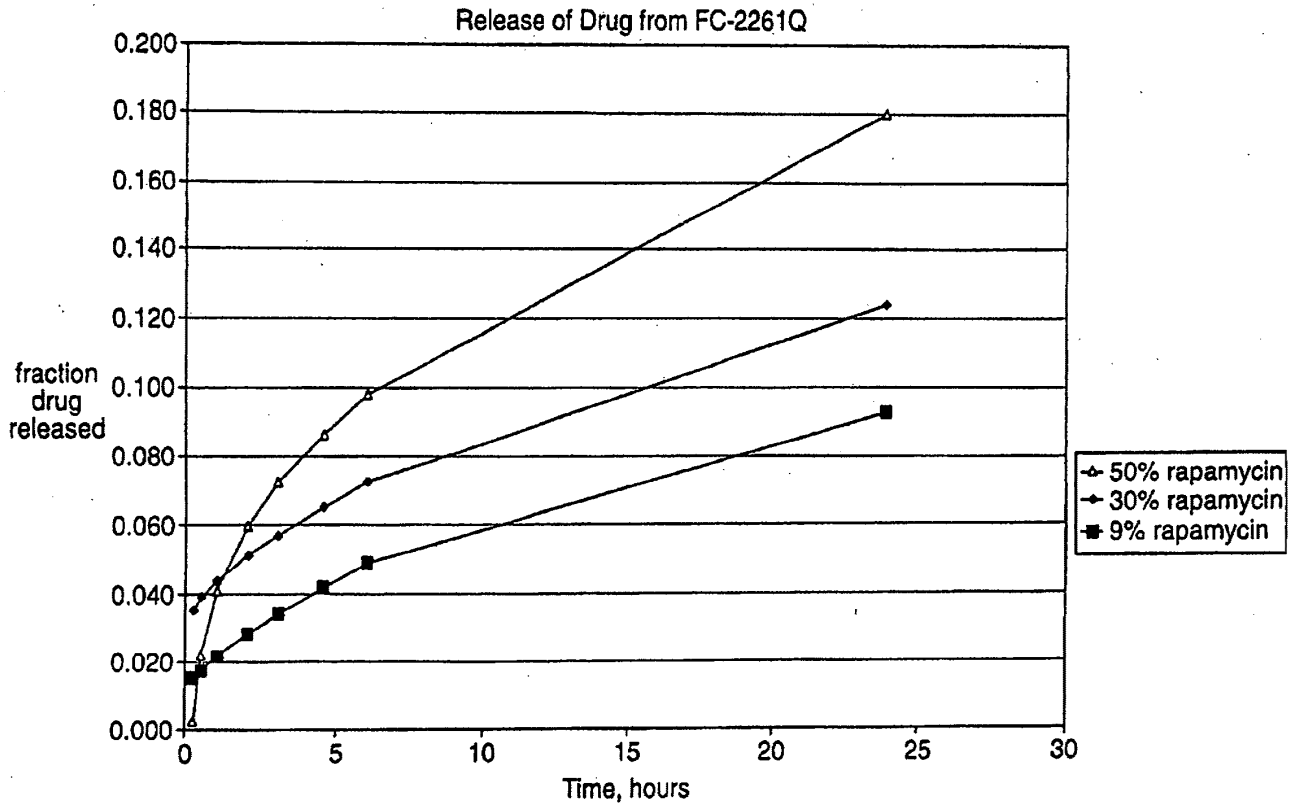

Release of Drug from FC-2261Q
fraction drug released
0.200
0.180
0.160
0.140
0.120
0.100
0.080
0.060
0.040
0.020
0.000
0
5
10
15
20
25
30
Time, hours
50% rapamycin
30% rapamycin
9% rapamycin

FIG. 6

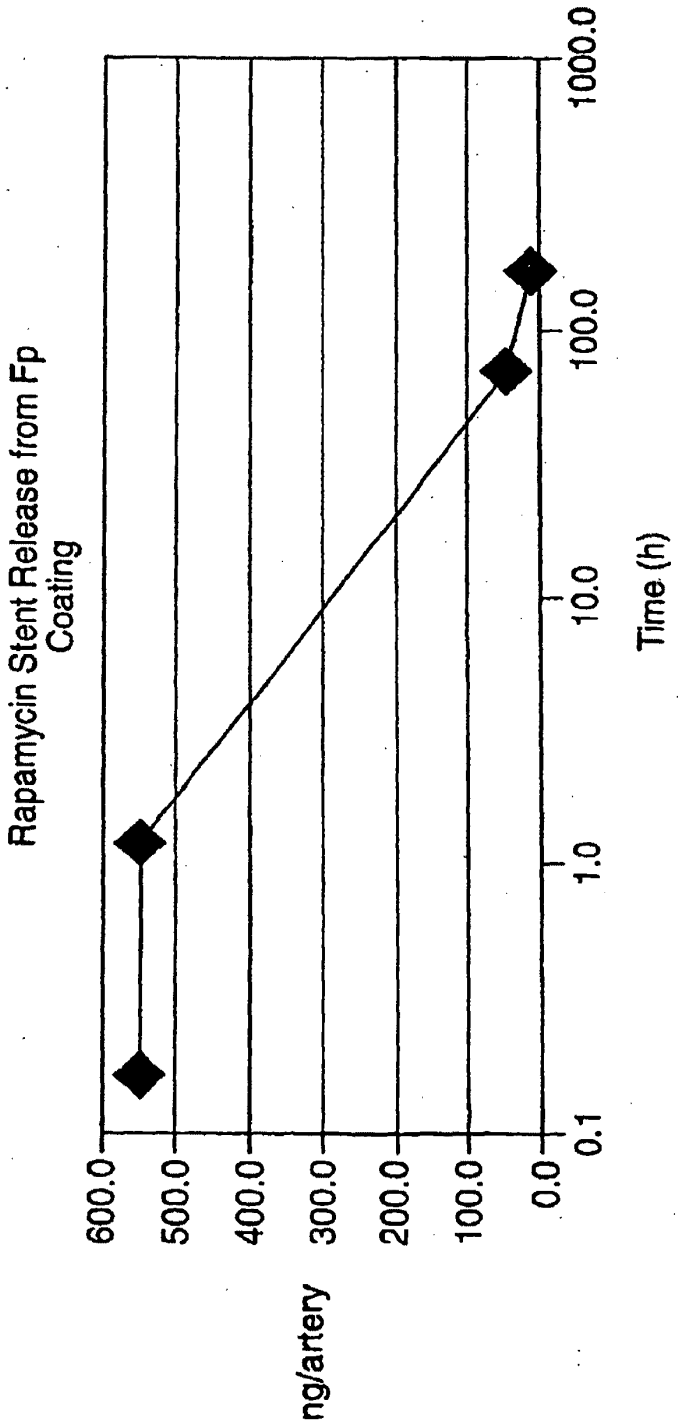

Rapamycin Stent Release from Fp Coating
ng/artery
600.0
500.0
400.0
300.0
200.0
100.0
0.0
0.1
1.0
10.0
100.0
1000.0
Time (h)

FIG. 7

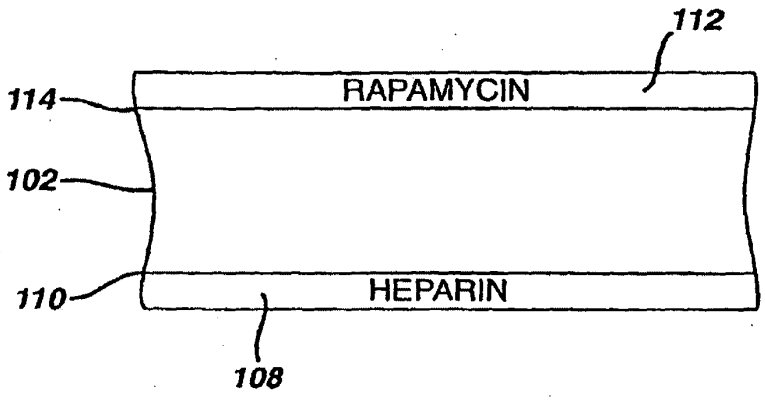


FIG. 8

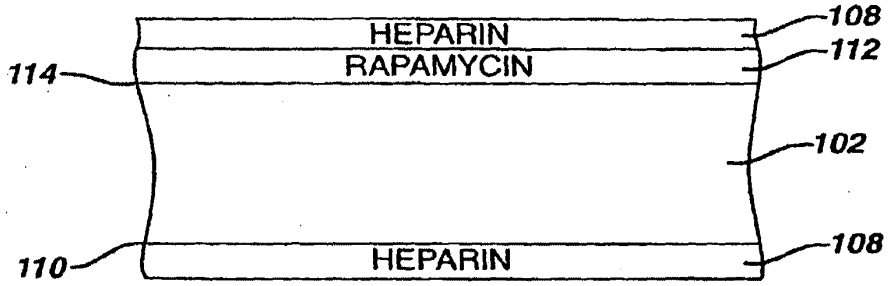
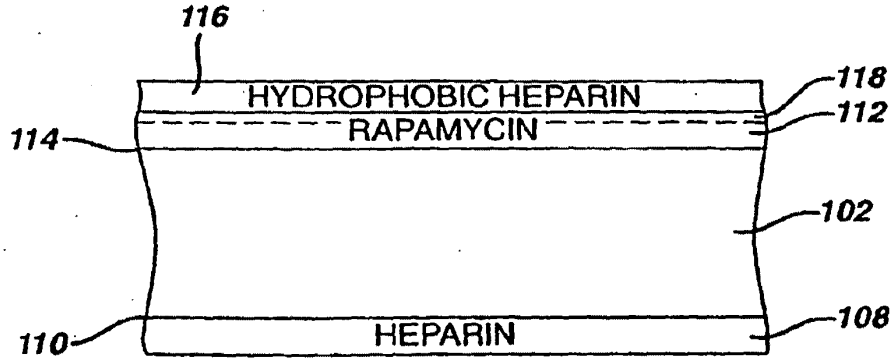


FIG. 9



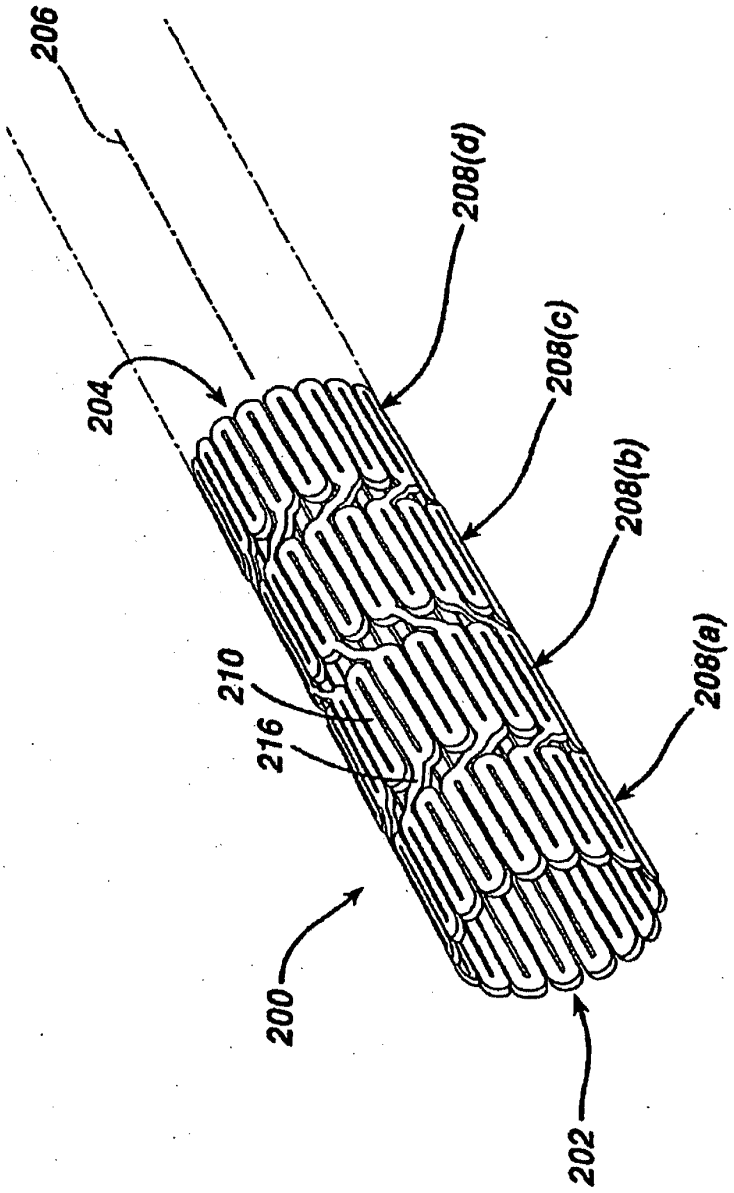


FIG. 10

FIG. 11

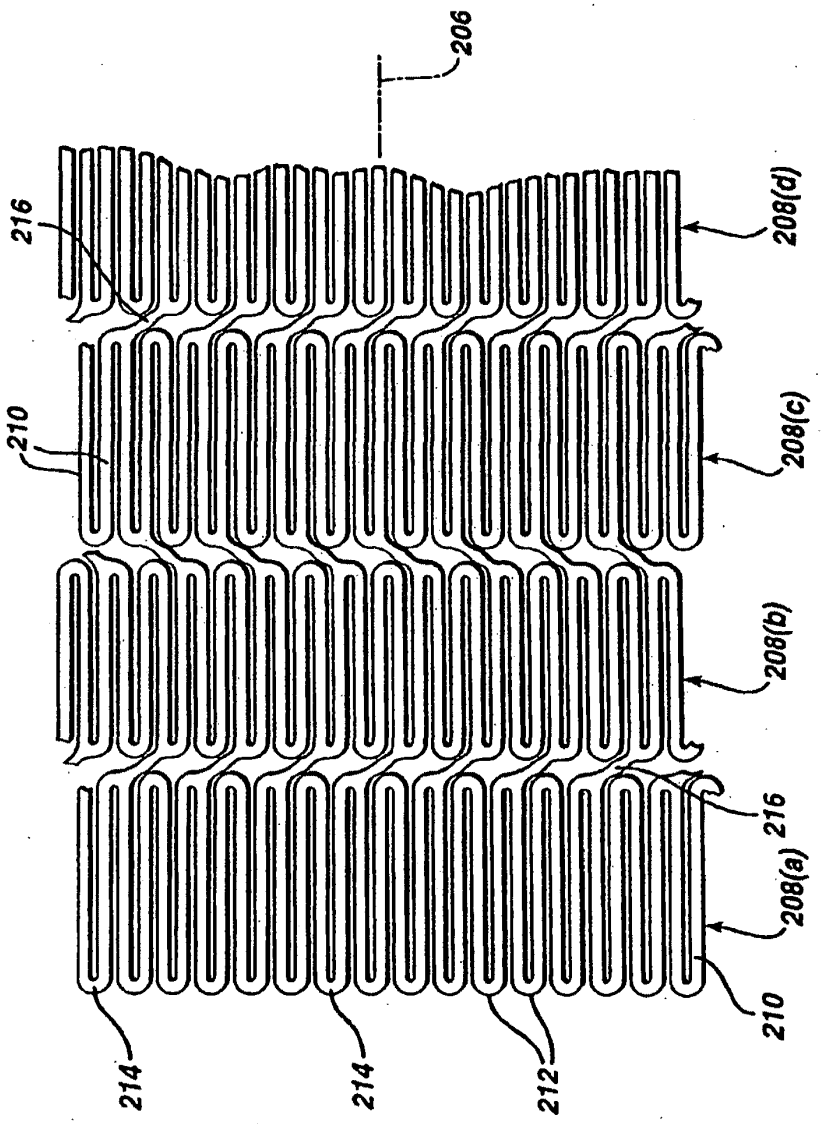


FIG. 12

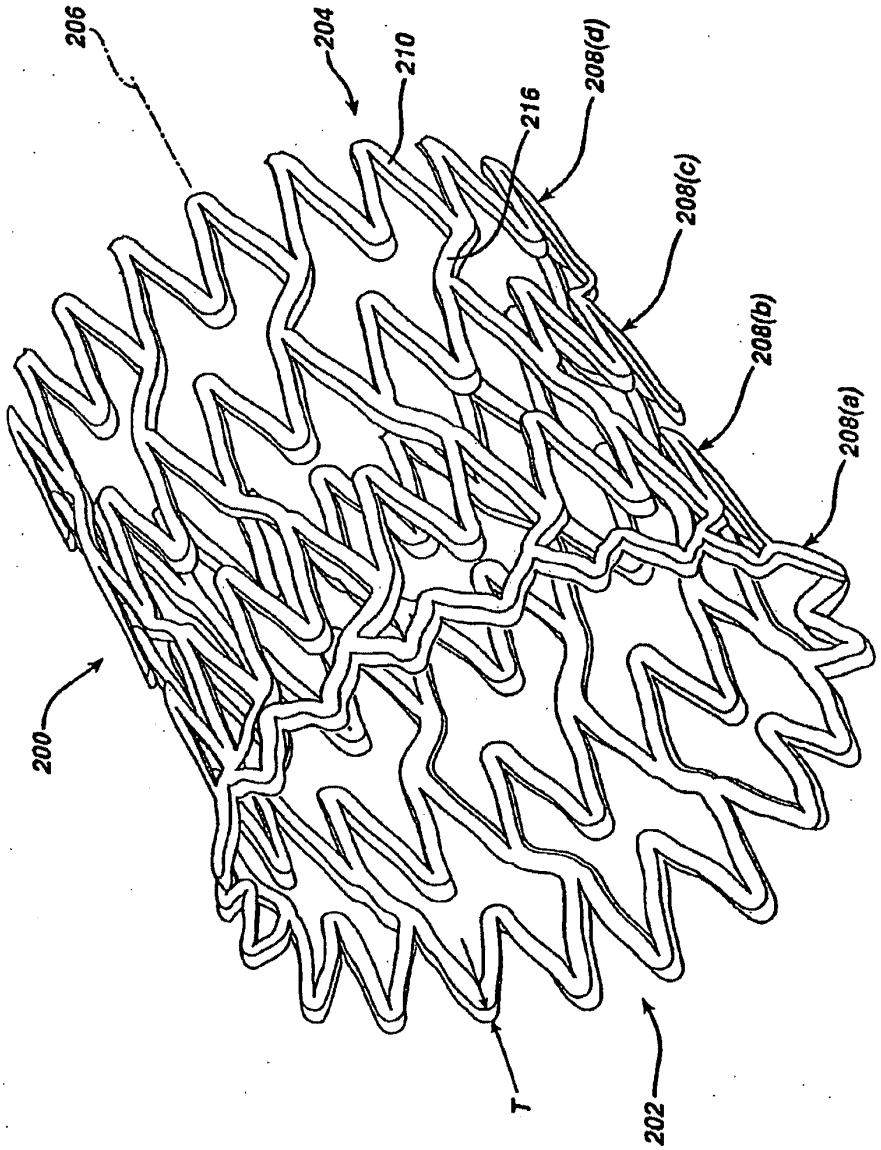


FIG. 13

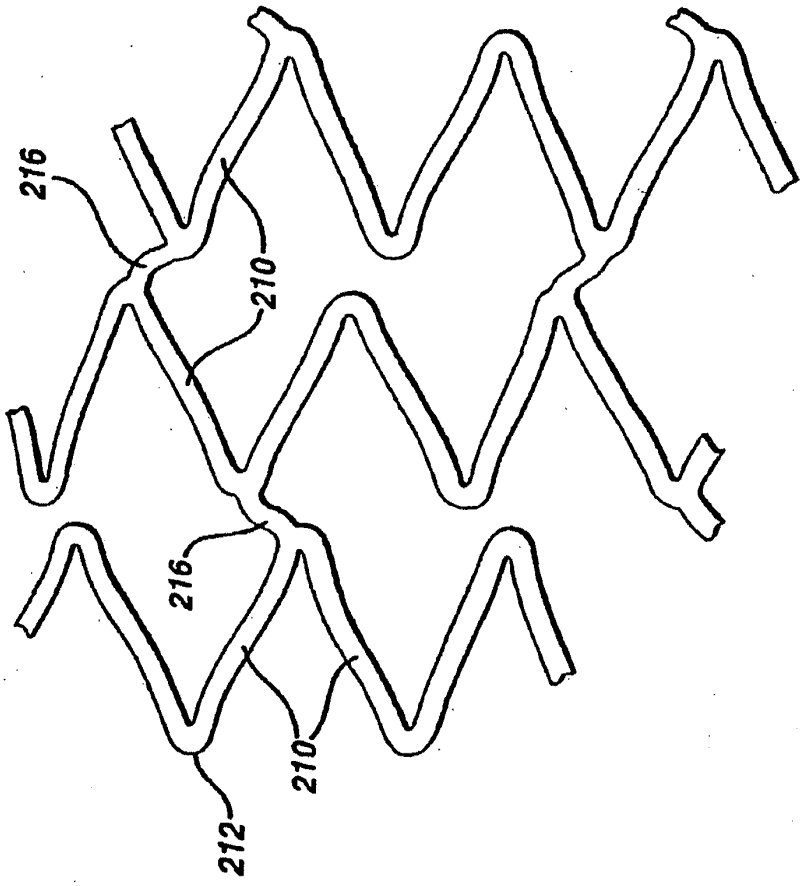
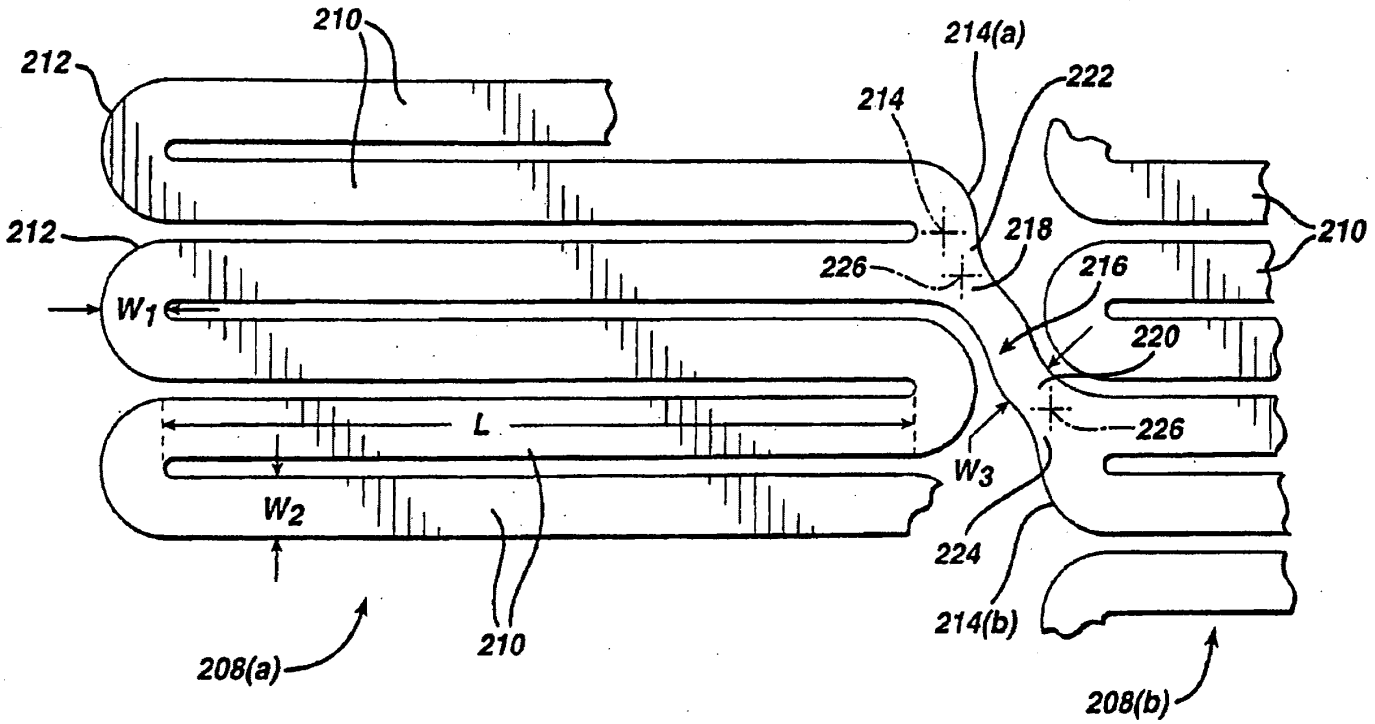


FIG. 14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W_3
W_2
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214(b)
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208(b)

FIG. 15

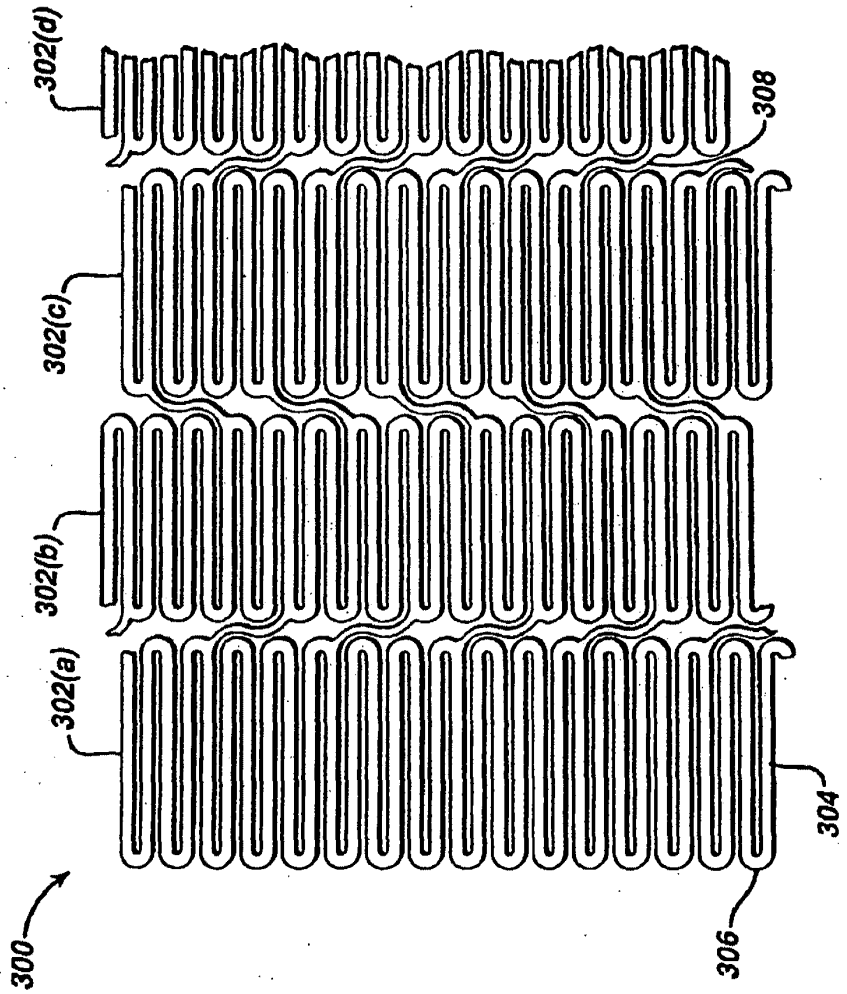

FIG. 16

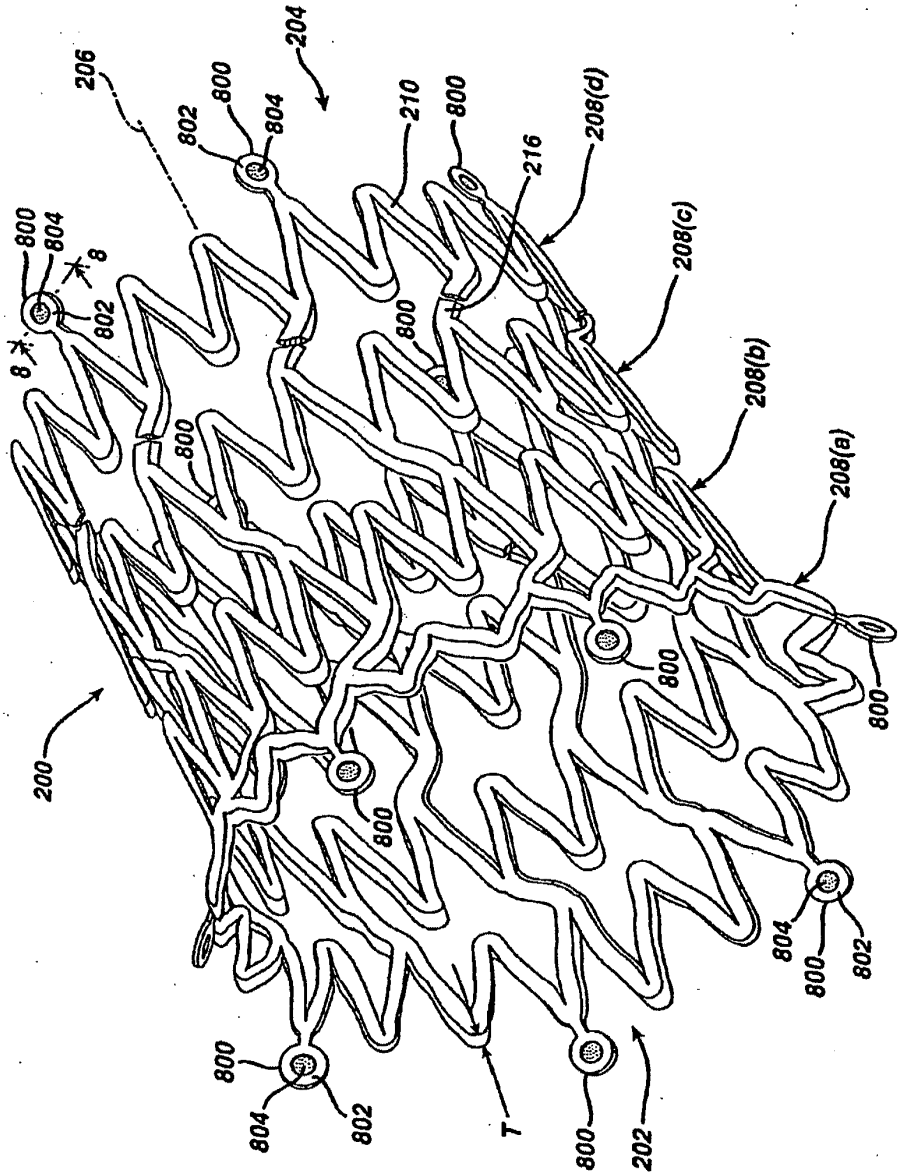
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FIG. 17

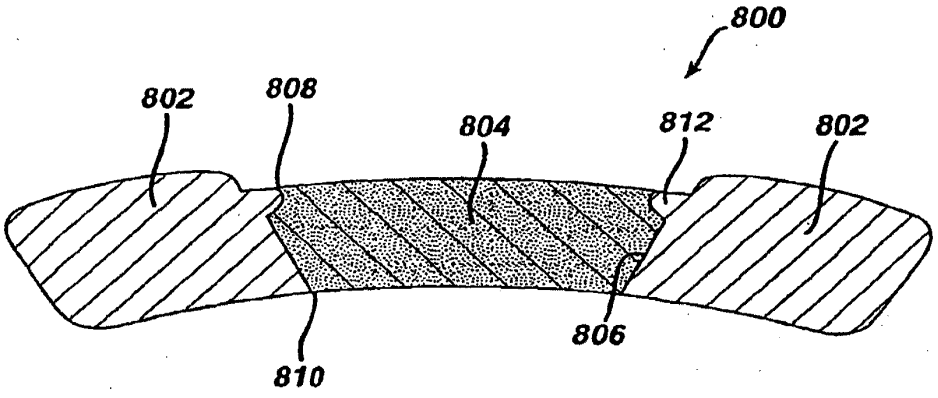
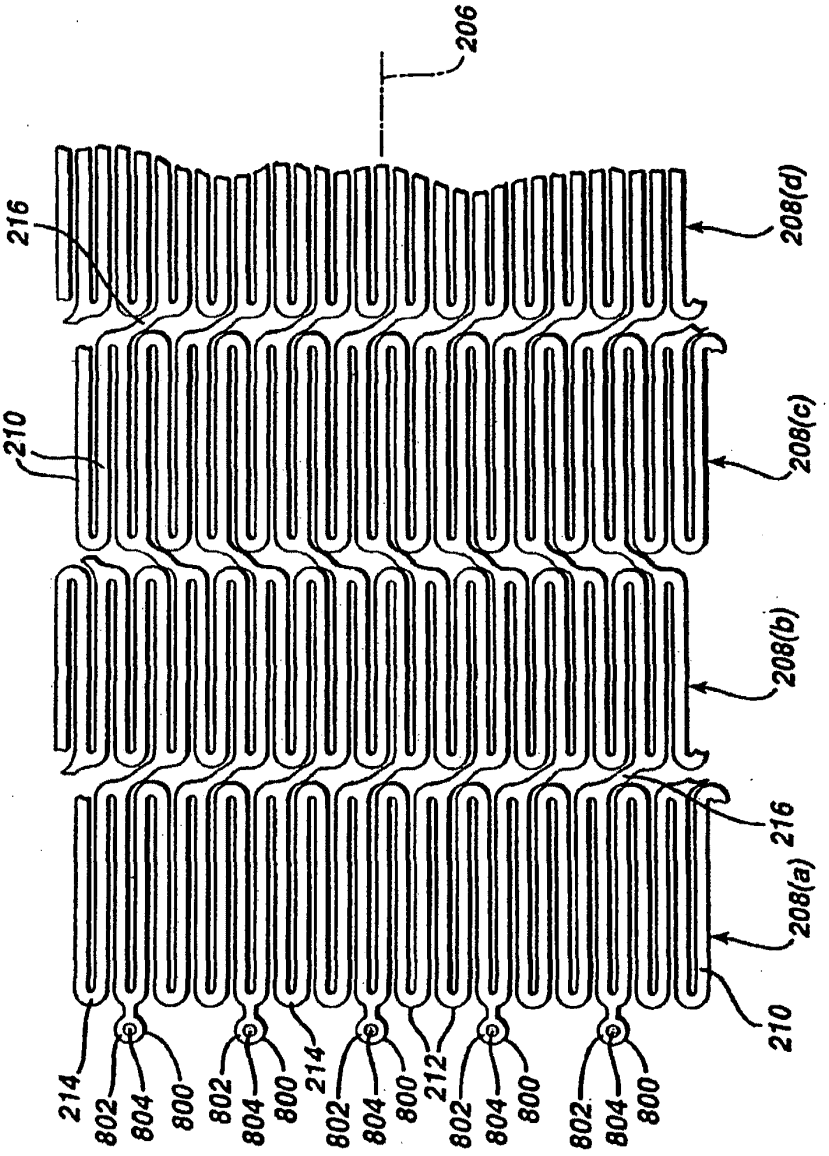


FIG. 18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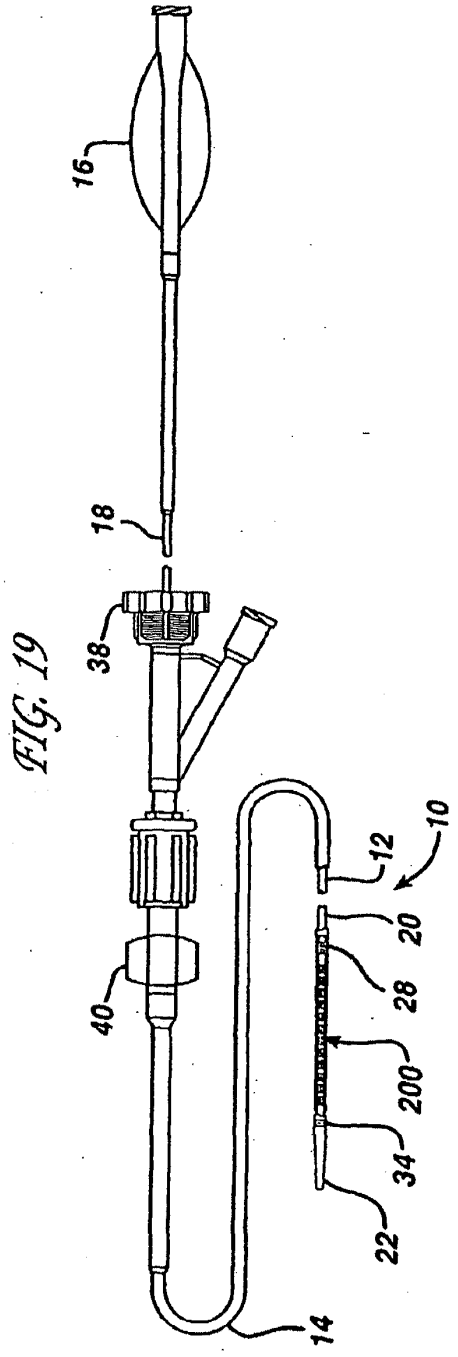
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FIG. 19

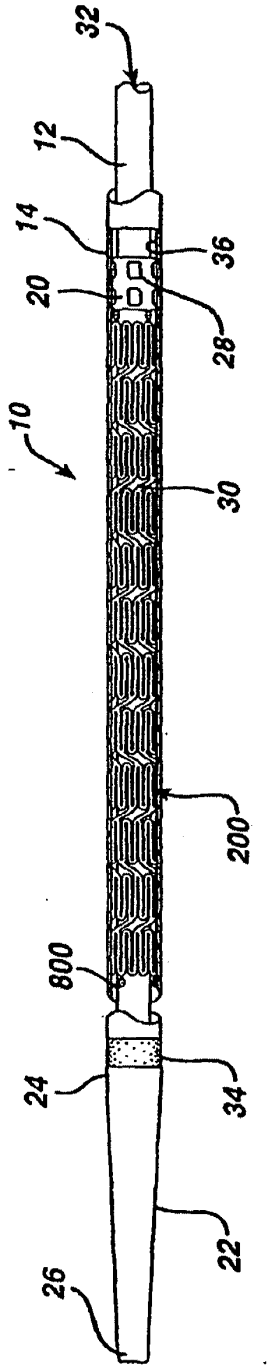
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FIG. 20

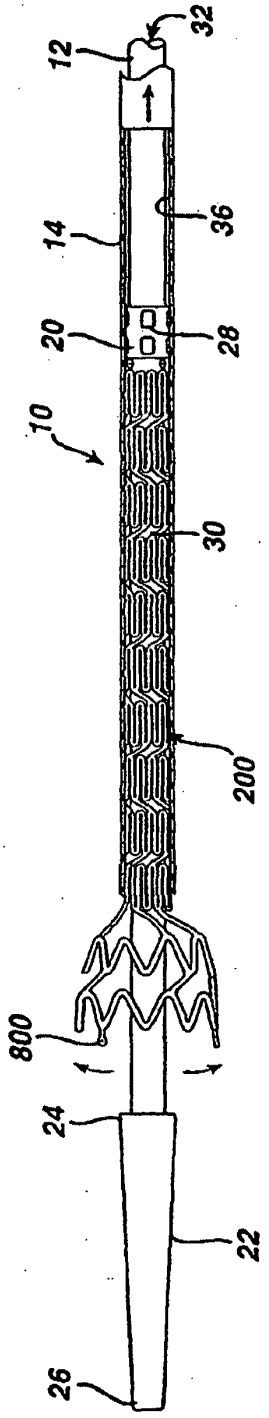


FIG. 21

FIG. 22

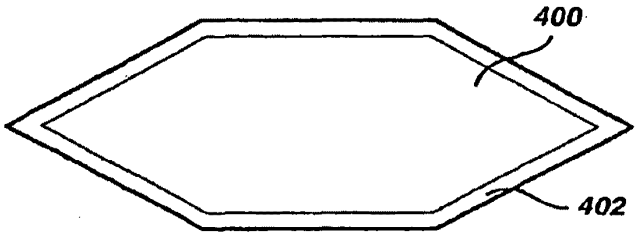


FIG. 23

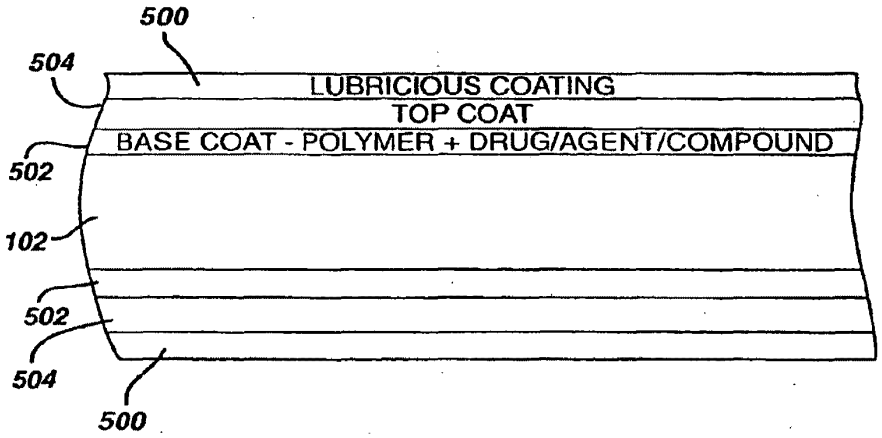


FIG. 24

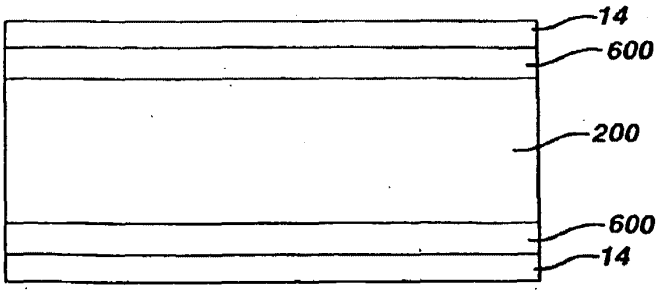


FIG. 25

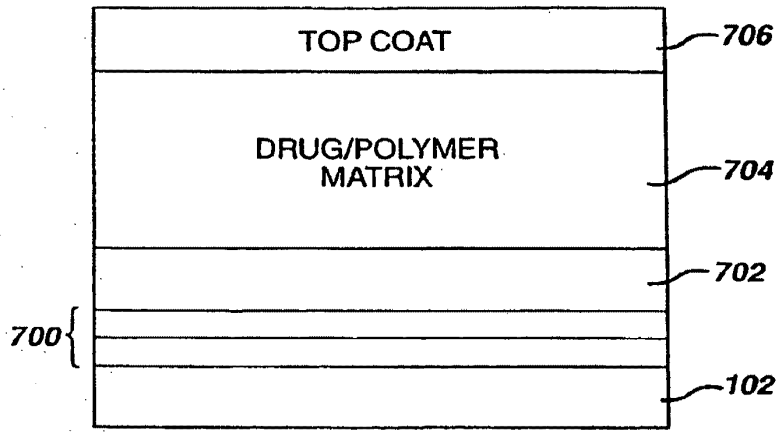
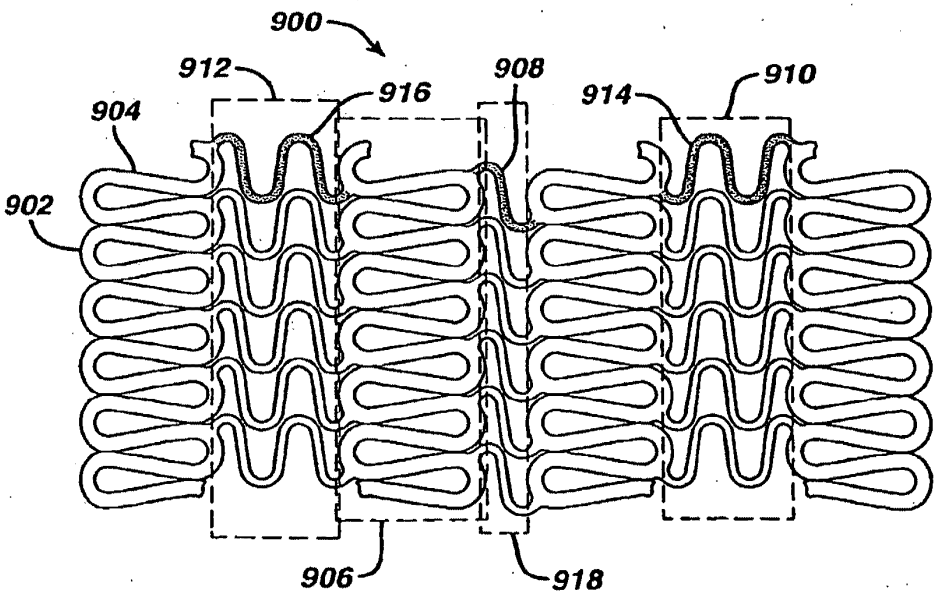

TOP COAT
706
DRUG/POLYMER MATRIX
704
702
700
102

FIG. 26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MEDICAL DEVICES, DRUG COATINGS AND METHODS FOR MAINTAINING THE DRUG COATINGS THEREON

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation application of U.S. Ser. No. 11/782,770, filed Jul. 25, 2007 (abandoned), which in turn is a continuation of U.S. Ser. No. 11/437,572, filed May 19, 2006, which is in turn a continuation of U.S. Ser. No. 10/636,435 filed Aug. 7, 2003, now U.S. Pat. No. 7,056,550, which is a continuation application of U.S. Ser. No. 09/962,496 filed Sep. 25, 2001 (abandoned), which is a continuation-in-part application of U.S. application Ser. No. 09/675,882, filed Sep. 29, 2000 (abandoned).

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to the local administration of drug/drug combinations for the prevention and treatment of vascular disease, and more particularly to intraluminal medical devices for the local delivery of drug/drug combinations for the prevention and treatment of vascular disease caused by injury and methods for maintaining the drug/drug combinations on the intraluminal medical devices. The present invention also relates to medical devices having drugs, agents or compounds affixed thereto to minimize or substantially eliminate a biological organism's reaction to the introduction of the medical device to the organism.

2. Discussion of the Related Art

Many individuals suffer from circulatory disease caused by a progressive blockage of the blood vessels that perfuse the heart and other major organs with nutrients. More severe blockage of blood vessels in such individuals often leads to hypertension, ischemic injury, stroke, or myocardial infarction. Atherosclerotic lesions, which limit or obstruct coronary blood flow, are the major cause of ischemic heart disease. Percutaneous transluminal coronary angioplasty is a medical procedure whose purpose is to increase blood flow through an artery. Percutaneous transluminal coronary angioplasty is the predominant treatment for coronary vessel stenosis. The increasing use of this procedure is attributable to its relatively high success rate and its minimal invasiveness compared with coronary bypass surgery. A limitation associated with percutaneous transluminal coronary angioplasty is the abrupt closure of the vessel which may occur immediately after the procedure and restenosis which occurs gradually following the procedure. Additionally, restenosis is a chronic problem in patients who have undergone saphenous vein bypass grafting. The mechanism of acute occlusion appears to involve several factors and may result from vascular recoil with resultant closure of the artery and/or deposition of blood platelets and fibrin along the damaged length of the newly opened blood vessel.

Restenosis after percutaneous transluminal coronary angioplasty is a more gradual process initiated by vascular injury. Multiple processes, including thrombosis, inflammation, growth factor and cytokine release, cell proliferation, cell migration and extracellular matrix synthesis each contribute to the restenotic process.

While the exact mechanism of restenosis is not completely understood, the general aspects of the restenosis process have been identified. In the normal arterial wall, smooth muscle cells proliferate at a low rate, approximately less than 0.1 percent per day. Smooth muscle cells in the vessel walls exist

in a contractile phenotype characterized by eighty to ninety percent of the cell cytoplasmic volume occupied with the contractile apparatus. Endoplasmic reticulum, Golgi, and free ribosomes are few and are located in the perinuclear region. Extracellular matrix surrounds the smooth muscle cells and is rich in heparin-like glycosylaminoglycans which are believed to be responsible for maintaining smooth muscle cells in the contractile phenotypic state (Campbell and Campbell, 1985).

Upon pressure expansion of an intracoronary balloon catheter during angioplasty, smooth muscle cells within the vessel wall become injured, initiating a thrombotic and inflammatory response. Cell derived growth factors such as platelet derived growth factor, basic fibroblast growth factor, epidermal growth factor, thrombin, etc., released from platelets, invading macrophages and/or leukocytes, or directly from the smooth muscle cells provoke a proliferative and migratory response in medial smooth muscle cells. These cells undergo a change from the contractile phenotype to a synthetic phenotype characterized by only a few contractile filament bundles, extensive rough endoplasmic reticulum, Golgi and free ribosomes. Proliferation/migration usually begins within one to two days post-injury and peaks several days thereafter (Campbell and Campbell, 1987; Clowes and Schwartz, 1985).

Daughter cells migrate to the intimal layer of arterial smooth muscle and continue to proliferate and secrete significant amounts of extracellular matrix proteins. Proliferation, migration and extracellular matrix synthesis continue until the damaged endothelial layer is repaired at which time proliferation slows within the intima, usually within seven to fourteen days post-injury. The newly formed tissue is called neointima. The further vascular narrowing that occurs over the next three to six months is due primarily to negative or constrictive remodeling.

Simultaneous with local proliferation and migration, inflammatory cells adhere to the site of vascular injury. Within three to seven days post-injury, inflammatory cells have migrated to the deeper layers of the vessel wall. In animal models employing either balloon injury or stent implantation, inflammatory cells may persist at the site of vascular injury for at least thirty days (Tanaka et al., 1993; Edelman et al., 1998). Inflammatory cells therefore are present and may contribute to both the acute and chronic phases of restenosis.

Numerous agents have been examined for presumed antiproliferative actions in restenosis and have shown some activity in experimental animal models. Some of the agents which have been shown to successfully reduce the extent of intimal hyperplasia in animal models include: heparin and heparin fragments (Clowes, A. W. and Karnovsky M., Nature 265: 25-26, 1977; Guyton, J. R. et al., Circ. Res., 46: 625-634, 1980; Clowes, A. W. and Clowes, M. M., Lab. Invest. 52: 611-616, 1985; Clowes, A. W. and Clowes, M. M., Circ. Res. 58: 839-845, 1986; Majesky et al., Circ. Res. 61: 296-300, 1987; Snow et al., Am. J. Pathol. 137: 313-330, 1990; Okada, T. et al., Neurosurgery 25: 92-98, 1989), colchicine (Currier, J. W. et al., Circ. 80: 11-66, 1989), taxol (Sollot, S. J. et al., J. Clin. Invest. 95: 1869-1876, 1995), angiotensin converting enzyme (ACE) inhibitors (Powell, J. S. et al., Science, 245: 186-188, 1989), angiopeptin (Lundergan, C. F. et al. Am. J. Cardiol. 17(Suppl. B):132B-136B, 1991), cyclosporin A (Jonasson, L. et al., Proc. Natl., Acad. Sci., 85: 2303, 1988), goat-anti-rabbit PDGF antibody (Ferns, G. A. A., et al., Science 253: 1129-1132, 1991), terbinafine (Nemecek, G. M. et al., J. Pharmacol. Exp. Thera. 248: 1167-1174, 1989), trapidil (Liu, M. W. et al., Circ. 81: 1089-1093, 1990), tranilast (Fuku-

yama, J. et al., Eur. J. Pharmacol. 318: 327-332, 1996), interferon-gamma (Hansson, G. K. and Holm, J., Circ. 84: 1266-1272, 1991), rapamycin (Marx, S. O. et al., Circ. Res. 76: 412-417, 1995), steroids (Colburn, M. D. et al., J. Vasc. Surg. 15: 510-518, 1992), see also Berk, B. C. et al., J. Am. Coll. Cardiol. 17: 111B-117B, 1991), ionizing radiation (Weinberger, J. et al., Int. J. Rad. Onc. Biol. Phys. 36: 767-775, 1996), fusion toxins (Farb, A. et al., Circ. Res. 80: 542-550, 1997) antisense oligionucleotides (Simons, M. et al., Nature 359: 67-70, 1992) and gene vectors (Chang, M. W. et al., J. Clin. Invest. 96: 2260-2268, 1995). Anti-proliferative action on smooth muscle cells in vitro has been demonstrated for many of these agents, including heparin and heparin conjugates, taxol, tranilast, colchicine, ACE inhibitors, fusion toxins, antisense oligionucleotides, rapamycin and ionizing radiation. Thus, agents with diverse mechanisms of smooth muscle cell inhibition may have therapeutic utility in reducing intimal hyperplasia.

However, in contrast to animal models, attempts in human angioplasty patients to prevent restenosis by systemic pharmacologic means have thus far been unsuccessful. Neither aspirin-dipyridamole, ticlopidine, anti-coagulant therapy (acute heparin, chronic warfarin, hirudin or hirulog), thromboxane receptor antagonism nor steroids have been effective in preventing restenosis, although platelet inhibitors have been effective in preventing acute reocclusion after angioplasty (Mak and Topol, 1997; Lang et al., 1991; Popma et al., 1991). The platelet GP II_b/III_a receptor, antagonist, Reopro® is still under study but Reopro® has not shown definitive results for the reduction in restenosis following angioplasty and stenting. Other agents, which have also been unsuccessful in the prevention of restenosis, include the calcium channel antagonists, prostacyclin mimetics, angiotensin converting enzyme inhibitors, serotonin receptor antagonists, and anti-proliferative agents. These agents must be given systemically, however, and attainment of a therapeutically effective dose may not be possible; anti-proliferative (or anti-restenosis) concentrations may exceed the known toxic concentrations of these agents so that levels sufficient to produce smooth muscle inhibition may not be reached (Mak and Topol, 1997; Lang et al., 1991; Popma et al., 1991).

Additional clinical trials in which the effectiveness for preventing restenosis utilizing dietary fish oil supplements or cholesterol lowering agents has been examined showing either conflicting or negative results so that no pharmacological agents are as yet clinically available to prevent post-angioplasty restenosis (Mak and Topol, 1997; Franklin and Faxon, 1993: Serruys, P. W. et al., 1993). Recent observations suggest that the antilipid/antioxident agent, probucol, may be useful in preventing restenosis but this work requires confirmation (Tardif et al., 1997; Yokoi, et al., 1997). Probucol is presently not approved for use in the United States and a thirty-day pretreatment period would preclude its use in emergency angioplasty. Additionally, the application of ionizing radiation has shown significant promise in reducing or preventing restenosis after angioplasty in patients with stents (Teirstein et al., 1997). Currently, however, the most effective treatments for restenosis are repeat angioplasty, atherectomy or coronary artery bypass grafting, because no therapeutic agents currently have Food and Drug Administration approval for use for the prevention of post-angioplasty restenosis.

Unlike systemic pharmacologic therapy, stents have proven useful in significantly reducing restenosis. Typically, stents are balloon-expandable slotted metal tubes (usually, but not limited to, stainless steel), which, when expanded within the lumen of an angioplastied coronary artery, provide structural support through rigid scaffolding to the arterial wall. This support is helpful in maintaining vessel lumen patency. In two randomized clinical trials, stents increased angiographic success after percutaneous transluminal coronary angioplasty, by increasing minimal lumen diameter and reducing, but not eliminating, the incidence of restenosis at six months (Serruys et al., 1994; Fischman et al., 1994).

Additionally, the heparin coating of stents appears to have the added benefit of producing a reduction in sub-acute thrombosis after stent implantation (Serruys et al., 1996). Thus, sustained mechanical expansion of a stenosed coronary artery with a stent has been shown to provide some measure of restenosis prevention, and the coating of stents with heparin has demonstrated both the feasibility and the clinical usefulness of delivering drugs locally, at the site of injured tissue.

As stated above, the use of heparin coated stents demonstrates the feasibility and clinical usefulness of local drug delivery; however, the manner in which the particular drug or drug combination is affixed to the local delivery device will play a role in the efficacy of this type of treatment. For example, the processes and materials utilized to affix the drug/drug combinations to the local delivery device should not interfere with the operations of the drug/drug combinations. In addition, the processes and materials utilized should be biocompatible and maintain the drug/drug combinations on the local device through delivery and over a given period of time. For example, removal of the drug/drug combination during delivery of the local delivery device may potentially cause failure of the device.

Accordingly, there exists a need for drug/drug combinations and associated local delivery devices for the prevention and treatment of vascular injury causing intimal thickening which is either biologically induced, for example atherosclerosis, or mechanically induced, for example, through percutaneous transluminal coronary angioplasty. In addition, there exists a need for maintaining the drug/drug combinations on the local delivery device through delivery and positioning as well as ensuring that the drug/drug combination is released in therapeutic dosages over a given period of time.

A variety of stent coatings and compositions have been proposed for the prevention and treatment of injury causing intimal thickening. The coatings may be capable themselves of reducing the stimulus the stent provides to the injured lumen wall, thus reducing the tendency towards thrombosis or restenosis. Alternately, the coating may deliver a pharmaceutical/therapeutic agent or drug to the lumen that reduces smooth muscle tissue proliferation or restenosis. The mechanism for delivery of the agent is through diffusion of the agent through either a bulk polymer or through pores that are created in the polymer structure, or by erosion of a biodegradable coating.

Both bioabsorbable and biostable compositions have been reported as coatings for stents. They generally have been polymeric coatings that either encapsulate a pharmaceutical/therapeutic agent or drug, e.g. rapamycin, taxol etc., or bind such an agent to the surface, e.g. heparin-coated stents. These coatings are applied to the stent in a number of ways, including, though not limited to, dip, spray, or spin coating processes.

One class of biostable materials that has been reported as coatings for stents is polyfluoro homopolymers. Polytetrafluoroethylene (PTFE) homopolymers have been used as implants for many years. These homopolymers are not soluble in any solvent at reasonable temperatures and there-

fore are difficult to coat onto small medical devices while maintaining important features of the devices (e.g. slots in stents).

Stents with coatings made from polyvinylidenefluoride homopolymers and containing pharmaceutical/therapeutic agents or drugs for release have been suggested. However, like most crystalline polyfluoro homopolymers, they are difficult to apply as high quality films onto surfaces without subjecting them to relatively high temperatures, that correspond to the melting temperature of the polymer.

It would be advantageous to develop coatings for implantable medical devices that will reduce thrombosis, restenosis, or other adverse reactions, that may include, but do not require, the use of pharmaceutical or therapeutic agents or drugs to achieve such affects, and that possess physical and mechanical properties effective for use in such devices even when such coated devices are subjected to relatively low maximum temperatures.

SUMMARY OF THE INVENTION

The drug/drug combination therapies, drug/drug combination carriers and associated local delivery devices of the present invention provide a means for overcoming the difficulties associated with the methods and devices currently in use, as briefly described above. In addition, the methods for maintaining the drug/drug combinations and drug/drug combination carriers on the local delivery device ensure that the drug/drug combination therapies reach the target site.

In accordance with one aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The device comprises a biocompatible vehicle affixed to at least a portion of the medical device, and at least one agent in therapeutic dosages incorporated into the biocompatible vehicle for the treatment of reactions by the living organism caused by the medical device or the implantation thereof.

In accordance with another aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The device comprises a biocompatible vehicle affixed to at least a portion of the medical device, at least one agent in therapeutic dosages incorporated into the biocompatible vehicle for the treatment of reactions by the living organism caused by the medical device or the implantation thereof, and a material for preventing the at least one agent from separating from the medical device prior to and during implantation of the medical device at the treatment site, the material being affixed to at least one of the medical devices or a delivery system for the medical device.

In accordance with another aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The device comprises a stent, a biocompatible vehicle affixed to at least a portion of the stent, and at least one agent in therapeutic dosages incorporated into the biocompatible vehicle for the treatment of reactions by the living organism caused by the medical device or the implantation thereof.

In accordance with another aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The device comprises a stent having a substantially tubular member having open ends, and a first diameter for insertion into a lumen of a vessel and a second diameter for anchoring in the lumen of the vessel, a biocompatible vehicle affixed to at least a portion of the stent, at least one agent in therapeutic dosages incorporated into the biocompatible vehicle for the treatment of reactions by the living organism caused by the medical device or the implantation thereof, and a material for preventing the at least one agent from separating from the medical device prior to and during implantation of the medical device at the treatment site, the material being affixed to at least one of the medical devices or a delivery system for the medical device.

In accordance with another aspect, the present invention is directed to a local drug delivery device. The device comprises a stent having a substantially tubular member having open ends, and a first diameter for insertion into a lumen of a vessel and a second diameter for anchoring in the lumen of a vessel, a biocompatible polymeric vehicle affixed to at least a portion of the stent, and rapamycin, in therapeutic dosages, incorporated into the biocompatible polymeric vehicle.

In accordance with another aspect, the present invention is directed to a method of coating a medical device with a therapeutic agent. The method comprises the steps of creating a polymer utilizing vinylidene fluoride and hexafluoropropylene in a batch emulsion polymerization process, priming the medical device with the polymer utilizing a dip coating process, creating a polymer and therapeutic agent mixture, applying the polymer and therapeutic agent mixture on the primer layer utilizing a spin coating process, and drying the medical device in a vacuum oven for approximately sixteen hours at a temperature in the range of fifty to sixty degrees centigrade.

In accordance with another aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The medical device comprises a biocompatible vehicle affixed to at least a portion of the medical device, and at least one agent incorporated into the biocompatible vehicle. The at least one agent being designed to react with one or more chemicals produced by the living organism to treat reactions by the living organism caused by the medical device or the implantation thereof.

In accordance with another aspect, the present invention is directed to a medical device for implantation into the vasculature of a living organism. The medical device comprises a self-expanding stent, a biocompatible vehicle affixed to at least a portion of the stent, and rapamycin, in therapeutic dosages, incorporated into the biocompatible vehicle for the prevention of restenosis.

In accordance with another aspect, the present invention is directed to a method of coating a medical device with a therapeutic agent. The method comprises the steps of creating a polymer utilizing vinylidene fluoride and hexafluoropropylene, adding one or more therapeutic agents to the polymer to create a polymer and therapeutic agent mixture, and applying the polymer and therapeutic agent mixture to the medical device.

In accordance with another aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The medical device comprises a biocompatible vehicle affixed to at least a portion of the medical device, at least one agent in therapeutic dosages incorporated into the biocompatible vehicle for the treatment of disease proximate the implantation site.

In accordance with another aspect, the present invention is directed to a medical device for implantation into a treatment site of a living organism. The medical device comprises a biocompatible vehicle affixed to at least a portion of the medical device, at least one agent in therapeutic dosages incorporated into the biocompatible vehicle for the treatment of disease remote from the implantation site.

The medical devices, drug coatings and methods for maintaining the drug coatings or vehicles thereon of the present invention utilizes a combination of materials to treat disease, and reactions by living organisms due to the implantation of

medical devices for the treatment of disease or other conditions. The local delivery of drugs, agents or compounds generally substantially reduces the potential toxicity of the drugs, agents or compounds when compared to systemic delivery while increasing their efficacy.

Drugs, agents or compounds may be affixed to any number of medical devices to treat various diseases. The drugs, agents or compounds may also be affixed to minimize or substantially eliminate the biological organism's reaction to the introduction of the medical device utilized to treat a separate condition. For example, stents may be introduced to open coronary arteries or other body lumens such as biliary ducts. The introduction of these stents cause a smooth muscle cell proliferation effect as well as inflammation. Accordingly, the stents may be coated with drugs, agents or compounds to combat these reactions.

The drugs, agents or compounds will vary depending upon the type of medical device, the reaction to the introduction of the medical device and/or the disease sought to be treated. The type of coating or vehicle utilized to immobilize the drugs, agents or compounds to the medical device may also vary depending on a number of factors, including the type of medical device, the type of drug, agent or compound and the rate of release thereof.

In order to be effective, the drugs, agents or compounds should preferably remain on the medical devices during delivery and implantation. Accordingly, various coating techniques for creating strong bonds between the drugs, agents or compounds may be utilized. In addition, various materials may be utilized as surface modifications to prevent the drugs, agents or compounds from coming off prematurely.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other features and advantages of the invention will be apparent from the following, more particular description of preferred embodiments of the invention, as illustrated in the accompanying drawings.

FIG. 1 is a view along the length of a stent (ends not shown) prior to expansion showing the exterior surface of the stent and the characteristic banding pattern.

FIG. 2 is a view along the length of the stent of FIG. 1 having reservoirs in accordance with the present invention.

FIG. 3 indicates the fraction of drug released as a function of time from coatings of the present invention over which no topcoat has been disposed.

FIG. 4 indicates the fraction of drug released as a function of time from coatings of the present invention including a topcoat disposed thereon.

FIG. 5 indicates the fraction of drug released as a function of time from coatings of the present invention over which no topcoat has been disposed.

FIG. 6 indicates in vivo stent release kinetics of rapamycin from poly(VDF/HFP).

FIG. 7 is a cross-sectional view of a band of the stent of FIG. 1 having drug coatings thereon in accordance with a first exemplary embodiment of the invention.

FIG. 8 is a cross-sectional view of a band of the stent of FIG. 1 having drug coatings thereon in accordance with a second exemplary embodiment of the invention.

FIG. 9 is a cross-sectional view of a band of the stent of FIG. 1 having drug coatings thereon in accordance with a third exemplary embodiment of the present invention.

FIG. 10 is a perspective view of an exemplary stent in its compressed state which may be utilized in conjunction with the present invention.

FIG. 11 is a sectional, flat view of the stent shown in FIG. 10.

FIG. 12 is a perspective view of the stent shown in FIG. 10 but showing it in its expanded state.

FIG. 13 is an enlarged sectional view of the stent shown in FIG. 12.

FIG. 14 is an enlarged view of section of the stent shown in FIG. 11.

FIG. 15 is a view similar to that of FIG. 11 but showing an alternate embodiment of the stent.

FIG. 16 is a perspective view of the stent of FIG. 10 having a plurality of markers attached to the ends thereof in accordance with the present invention.

FIG. 17 is a cross-sectional view of a marker in accordance with the present invention.

FIG. 18 is an enlarged perspective view of an end of the stent with the markers forming a substantially straight line in accordance with the present invention.

FIG. 19 is a simplified partial cross-sectional view of a stent delivery apparatus having a stent loaded therein, which can be used with a stent made in accordance with the present invention.

FIG. 20 is a view similar to that of FIG. 19 but showing an enlarged view of the distal end of the apparatus.

FIG. 21 is a perspective view of an end of the stent with the markers in a partially expanded form as it emerges from the delivery apparatus in accordance with the present invention.

FIG. 22 is a cross-sectional view of a balloon having a lubricious coating affixed thereto in accordance with the present invention.

FIG. 23 is a cross-sectional view of a band of the stent in FIG. 1 having a lubricious coating affixed thereto in accordance with the present invention.

FIG. 24 is a cross-sectional view of a self-expanding stent in a delivery device having a lubricious coating in accordance with the present invention.

FIG. 25 is a cross-sectional view of a band of the stent in FIG. 1 having a modified polymer coating in accordance with the present invention.

FIG. 26 illustrates an exemplary balloon-expandable stent having an alternative arrangement of "N" and "J" links between sets of strut members, represented on a flat, two-dimensional plan view in accordance with the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The drug/drug combinations and delivery devices of the present invention may be utilized to effectively prevent and treat vascular disease, and in particular, vascular disease caused by injury. Various medical treatment devices utilized in the treatment of vascular disease may ultimately induce further complications. For example, balloon angioplasty is a procedure utilized to increase blood flow through an artery and is the predominant treatment for coronary vessel stenosis. However, as stated above, the procedure typically causes a certain degree of damage to the vessel wall, thereby potentially exacerbating the problem at a point later in time. Although other procedures and diseases may cause similar injury, exemplary embodiments of the present invention will be described with respect to the treatment of restenosis and related complications following percutaneous transluminal coronary angioplasty and other similar arterial/venous procedures.

While exemplary embodiments of the invention will be described with respect to the treatment of restenosis and

related complications following percutaneous transluminal coronary angioplasty, it is important to note that the local delivery of drug/drug combinations may be utilized to treat a wide variety of conditions utilizing any number of medical devices, or to enhance the function and/or life of the device. For example, intraocular lenses, placed to restore vision after cataract surgery is often compromised by the formation of a secondary cataract. The latter is often a result of cellular overgrowth on the lens surface and can be potentially minimized by combining a drug or drugs with the device. Other medical devices which often fail due to tissue in-growth or accumulation of proteinaceous material in, on and around the device, such as shunts for hydrocephalus, dialysis grafts, colostomy bag attachment devices, ear drainage tubes, leads for pace makers and implantable defibrillators can also benefit from the device-drug combination approach.

Devices which serve to improve the structure and function of tissue or organ may also show benefits when combined with the appropriate agent or agents. For example, improved osteointegration of orthopedic devices to enhance stabilization of the implanted device could potentially be achieved by combining it with agents such as bone-morphogenic protein. Similarly other surgical devices, sutures, staples, anastomosis devices, vertebral disks, bone pins, suture anchors, hemostatic barriers, clamps, screws, plates, clips, vascular implants, tissue adhesives and sealants, tissue scaffolds, various types of dressings, bone substitutes, intraluminal devices, and vascular supports could also provide enhanced patient benefit using this drug-device combination approach. Essentially, any type of medical device may be coated in some fashion with a drug or drug combination which enhances treatment over use of the singular use of the device or pharmaceutical agent.

In addition to various medical devices, the coatings on these devices may be used to deliver therapeutic and pharmaceutic agents including: antiproliferative/antimitotic agents including natural products such as vinca alkaloids (i.e. vinblastine, vincristine, and vinorelbine), paclitaxel, epidipodophyllotoxins (i.e. etoposide, teniposide), antibiotics (dactinomycin (actinomycin D) daunorubicin, doxorubicin and idarubicin), anthracyclines, mitoxantrone, bleomycins, plicamycin (mithramycin) and mitomycin, enzymes (L-asparaginase which systemically metabolizes L-asparagine and deprives cells which do not have the capacity to synthesize their own asparagine); antiplatelet agents such as G(GP)I-$I_b$$III_a$ inhibitors and vitronectin receptor antagonists; antiproliferative/antimitotic alkylating agents such as nitrogen mustards (mechlorethamine, cyclophosphamide and analogs, melphalan, chlorambucil), ethylenimines and methylmelamines (hexamethylmelamine and thiotepa), alkyl sulfonates-busulfan, nirtosoureas (carmustine (BCNU) and analogs, streptozocin), trazenes-dacarbazinine (DTIC); antiproliferative/antimitotic antimetabolites such as folic acid analogs (methotrexate), pyrimidine analogs (fluorouracil, floxuridine, and cytarabine), purine analogs and related inhibitors (mercaptopurine, thioguanine, pentostatin and 2-chlorodeoxyadenosine {cladribine}); platinum coordination complexes (cisplatin, carboplatin), procarbazine, hydroxyurea, mitotane, aminoglutethimide; hormones (i.e. estrogen); anticoagulants (heparin, synthetic heparin salts and other inhibitors of thrombin); fibrinolytic agents (such as tissue plasminogen activator, streptokinase and urokinase), aspirin, dipyridamole, ticlopidine, clopidogrel, abciximab; antimigratory; antisecretory (breveldin); antiinflammatory: such as adrenocortical steroids (cortisol, cortisone, fludrocortisone, prednisone, prednisolone, 6α-methylprednisolone, triamcinolone, betamethasone, and dexamethasone), non-steroidal agents (salicylic acid derivatives i.e. aspirin; para-aminophenol derivatives i.e. acetominophen; indole and indene acetic acids (indomethacin, sulindac, and etodalac), heteroaryl acetic acids (tolmetin, diclofenac, and ketorolac), arylpropionic acids (ibuprofen and derivatives), anthranilic acids (mefenamic acid, and meclofenamic acid), enolic acids (piroxicam, tenoxicam, phenylbutazone, and oxyphenthatrazone), nabumetone, gold compounds (auranofin, aurothioglucose, gold sodium thiomalate); immunosuppressives: (cyclosporine, tacrolimus (FK-506), sirolimus (rapamycin), azathioprine, mycophenolate mofetil); angiogenic agents: vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF); angiotensin receptor blocker; nitric oxide donors; anti-sense oligionucleotides and combinations thereof; cell cycle inhibitors, mTOR inhibitors, and growth factor signal transduction kinase inhibitors.

As stated previously, the implantation of a coronary stent in conjunction with balloon angioplasty is highly effective in treating acute vessel closure and may reduce the risk of restenosis. Intravascular ultrasound studies (Mintz et al., 1996) suggest that coronary stenting effectively prevents vessel constriction and that most of the late luminal loss after stent implantation is due to plaque growth, probably related to neointimal hyperplasia. The late luminal loss after coronary stenting is almost two times higher than that observed after conventional balloon angioplasty. Thus, inasmuch as stents prevent at least a portion of the restenosis process, a combination of drugs, agents or compounds which prevents smooth muscle cell proliferation, reduces inflammation and reduces coagulation or prevents smooth muscle cell proliferation by multiple mechanisms, reduces inflammation and reduces coagulation combined with a stent may provide the most efficacious treatment for post-angioplasty restenosis. The systemic use of drugs, agents or compounds in combination with the local delivery of the same or different drug/drug combinations may also provide a beneficial treatment option.

The local delivery of drug/drug combinations from a stent has the following advantages; namely, the prevention of vessel recoil and remodeling through the scaffolding action of the stent and the prevention of multiple components of neointimal hyperplasia or restenosis as well as a reduction in inflammation and thrombosis. This local administration of drugs, agents or compounds to stented coronary arteries may also have additional therapeutic benefit. For example, higher tissue concentrations of the drugs, agents or compounds may be achieved utilizing local delivery, rather than systemic administration. In addition, reduced systemic toxicity may be achieved utilizing local delivery rather than systemic administration while maintaining higher tissue concentrations. Also in utilizing local delivery from a stent rather than systemic administration, a single procedure may suffice with better patient compliance. An additional benefit of combination drug, agent, and/or compound therapy may be to reduce the dose of each of the therapeutic drugs, agents or compounds, thereby limiting their toxicity, while still achieving a reduction in restenosis, inflammation and thrombosis. Local stent-based therapy is therefore a means of improving the therapeutic ratio (efficacy/toxicity) of anti-restenosis, anti-inflammatory, anti-thrombotic drugs, agents or compounds.

There are a multiplicity of different stents that may be utilized following percutaneous transluminal coronary angioplasty. Although any number of stents may be utilized in accordance with the present invention, for simplicity, a limited number of stents will be described in exemplary embodiments of the present invention. The skilled artisan will recognize that any number of stents may be utilized in

connection with the present invention. In addition, as stated above, other medical devices may be utilized.

A stent is commonly used as a tubular structure left inside the lumen of a duct to relieve an obstruction. Commonly, stents are inserted into the lumen in a non-expanded form and are then expanded autonomously, or with the aid of a second device in situ. A typical method of expansion occurs through the use of a catheter-mounted angioplasty balloon which is inflated within the stenosed vessel or body passageway in order to shear and disrupt the obstructions associated with the wall components of the vessel and to obtain an enlarged lumen.

FIG. 1 illustrates an exemplary stent **100** which may be utilized in accordance with an exemplary embodiment of the present invention. The expandable cylindrical stent **100** comprises a fenestrated structure for placement in a blood vessel, duct or lumen to hold the vessel, duct or lumen open, more particularly for protecting a segment of artery from restenosis after angioplasty. The stent **100** may be expanded circumferentially and maintained in an expanded configuration, that is circumferentially or radially rigid. The stent **100** is axially flexible and when flexed at a band, the stent **100** avoids any externally-protruding component parts.

The stent **100** generally comprises first and second ends with an intermediate section therebetween. The stent **100** has a longitudinal axis and comprises a plurality of longitudinally disposed bands **102**, wherein each band **102** defines a generally continuous wave along a line segment parallel to the longitudinal axis. A plurality of circumferentially arranged links **104** maintain the bands **102** in a substantially tubular structure. Essentially, each longitudinally disposed band **102** is connected at a plurality of periodic locations, by a short circumferentially arranged link **104** to an adjacent band **102**. The wave associated with each of the bands **102** has approximately the same fundamental spatial frequency in the intermediate section, and the bands **102** are so disposed that the wave associated with them are generally aligned so as to be generally in phase with one another. As illustrated in the figure, each longitudinally arranged band **102** undulates through approximately two cycles before there is a link to an adjacent band **102**.

The stent **100** may be fabricated utilizing any number of methods. For example, the stent **100** may be fabricated from a hollow or formed stainless steel tube that may be machined using lasers, electric discharge milling, chemical etching or other means. The stent **100** is inserted into the body and placed at the desired site in an unexpanded form. In one exemplary embodiment, expansion may be effected in a blood vessel by a balloon catheter, where the final diameter of the stent **100** is a function of the diameter of the balloon catheter used.

It should be appreciated that a stent **100** in accordance with the present invention may be embodied in a shape-memory material, including, for example, an appropriate alloy of nickel and titanium or stainless steel. Structures formed from stainless steel may be made self-expanding by configuring the stainless steel in a predetermined manner, for example, by twisting it into a braided configuration. In this embodiment after the stent **100** has been formed it may be compressed so as to occupy a space sufficiently small as to permit its insertion in a blood vessel or other tissue by insertion means, wherein the insertion means include a suitable catheter, or flexible rod. On emerging from the catheter, the stent **100** may be configured to expand into the desired configuration where the expansion is automatic or triggered by a change in pressure, temperature or electrical stimulation.

FIG. 2 illustrates an exemplary embodiment of the present invention utilizing the stent **100** illustrated in FIG. 1. As illustrated, the stent **100** may be modified to comprise one or more reservoirs **106**. Each of the reservoirs **106** may be opened or closed as desired. These reservoirs **106** may be specifically designed to hold the drug/drug combinations to be delivered. Regardless of the design of the stent **100**, it is preferable to have the drug/drug combination dosage applied with enough specificity and a sufficient concentration to provide an effective dosage in the lesion area. In this regard, the reservoir size in the bands **102** is preferably sized to adequately apply the drug/drug combination dosage at the desired location and in the desired amount.

In an alternate exemplary embodiment, the entire inner and outer surface of the stent **100** may be coated with drug/drug combinations in therapeutic dosage amounts. A detailed description of a drug for treating restenosis, as well as exemplary coating techniques, is described below. It is, however, important to note that the coating techniques may vary depending on the drug/drug combinations. Also, the coating techniques may vary depending on the material comprising the stent or other intraluminal medical device.

FIG. 26 illustrates another exemplary embodiment of a balloon-expandable stent. FIG. 26 illustrates the stent **900** in its crimped, pre-deployed state as it would appear if it were cut longitudinally and then laid out into a flat, two-dimensional configuration. The stent **900** has curved end struts **902** and diagonal struts **904** with each set of strut members **906** connected by sets of flexible links **908**, **910** or **912**. In this exemplary embodiment, three different types of flexible links are used. A set of "N" links **910** comprising six circumferentially spaced "N" links **914** and a set of inverted "N" links **912** comprising six circumferentially spaced inverted "N" links **916** each connect to adjacent sets of strut members **906** at the ends of the stent **900**. A set of inverted "J" links **918** comprising six circumferentially spaced inverted "J" links **908** are used to connect the adjacent sets of strut members **906** in the center of the stent **900**. The shape of the "N" links **914** and inverted "N" links **916** facilitate the links' ability to lengthen and shorten as the stent bends around a curve during delivery into the human body. This ability to lengthen and shorten helps to prevent the sets of strut members from being pushed or pulled off the balloon during delivery into the body and is particularly applicable to short stents which tend to have relatively poor stent retention onto an inflatable balloon. The stent **900** with its greater strength at its central region would advantageously be used for comparatively short stenoses that have a tough, calcified central section. It should also be understood that a regular "J" link could be used for the stent **900** in place of the inverted "J" link **908**. Other exemplary embodiments of balloon expandable stents may be found in U.S. Pat. No. 6,190,403 B1 issued on Feb. 20, 2001 and which is incorporated by reference herein.

Rapamycin is a macrocyclic triene antibiotic produced by *Streptomyces hygroscopicus* as disclosed in U.S. Pat. No. 3,929,992. It has been found that rapamycin among other things inhibits the proliferation of vascular smooth muscle cells in vivo. Accordingly, rapamycin may be utilized in treating intimal smooth muscle cell hyperplasia, restenosis, and vascular occlusion in a mammal, particularly following either biologically or mechanically mediated vascular injury, or under conditions that would predispose a mammal to suffering such a vascular injury. Rapamycin functions to inhibit smooth muscle cell proliferation and does not interfere with the re-endothelialization of the vessel walls.

Rapamycin reduces vascular hyperplasia by antagonizing smooth muscle proliferation in response to mitogenic signals

that are released during an angioplasty induced injury. Inhibition of growth factor and cytokine mediated smooth muscle proliferation at the late G1 phase of the cell cycle is believed to be the dominant mechanism of action of rapamycin. However, rapamycin is also known to prevent T-cell proliferation and differentiation when administered systemically. This is the basis for its immunosuppresive activity and its ability to prevent graft rejection.

As used herein, rapamycin includes rapamycin and all analogs, derivatives and congeners that bind FKBP12, and other immunophilins, and possesses the same pharmacologic properties as rapamycin.

Although the anti-proliferative effects of rapamycin may be achieved through systemic use, superior results may be achieved through the local delivery of the compound. Essentially, rapamycin works in the tissues, which are in proximity to the compound, and has diminished effect as the distance from the delivery device increases. In order to take advantage of this effect, one would want the rapamycin in direct contact with the lumen walls. Accordingly, in a preferred embodiment, the rapamycin is incorporated onto the surface of the stent or portions thereof. Essentially, the rapamycin is preferably incorporated into the stent **100**, illustrated in FIG. 1, where the stent **100** makes contact with the lumen wall.

Rapamycin may be incorporated onto or affixed to the stent in a number of ways. In the exemplary embodiment, the rapamycin is directly incorporated into a polymeric matrix and sprayed onto the outer surface of the stent. The rapamycin elutes from the polymeric matrix over time and enters the surrounding tissue. The rapamycin preferably remains on the stent for at least three days up to approximately six months, and more preferably between seven and thirty days.

Any number of non-erodible polymers may be utilized in conjunction with the rapamycin. In one exemplary embodiment, the polymeric matrix comprises two layers. The base layer comprises a solution of poly(ethylene-co-vinylacetate) and polybutylmethacrylate. The rapamycin is incorporated into this base layer. The outer layer comprises only polybutylmethacrylate and acts as a diffusion barrier to prevent the rapamycin from eluting too quickly. The thickness of the outer layer or top coat determines the rate at which the rapamycin elutes from the matrix. Essentially, the rapamycin elutes from the matrix by diffusion through the polymer matrix. Polymers are permeable, thereby allowing solids, liquids and gases to escape therefrom. The total thickness of the polymeric matrix is in the range from about one micron to about twenty microns or greater. It is important to note that primer layers and metal surface treatments may be utilized before the polymeric matrix is affixed to the medical device. For example, acid cleaning, alkaline (base) cleaning, salinization and parylene deposition may be used as part of the overall process described below.

The poly(ethylene-co-vinylacetate), polybutylmethacrylate and rapamycin solution may be incorporated into or onto the stent in a number of ways. For example, the solution may be sprayed onto the stent or the stent may be dipped into the solution. Other methods include spin coating and RF-plasma polymerization. In one exemplary embodiment, the solution is sprayed onto the stent and then allowed to dry. In another exemplary embodiment, the solution may be electrically charged to one polarity and the stent electrically changed to the opposite polarity. In this manner, the solution and stent will be attracted to one another. In using this type of spraying process, waste may be reduced and more precise control over the thickness of the coat may be achieved.

In another exemplary embodiment, the rapamycin or other therapeutic agent may be incorporated into a film-forming polyfluoro copolymer comprising an amount of a first moiety selected from the group consisting of polymerized vinylidenefluoride and polymerized tetrafluoroethylene, and an amount of a second moiety other than the first moiety and which is copolymerized with the first moiety, thereby producing the polyfluoro copolymer, the second moiety being capable of providing toughness or elastomeric properties to the polyfluoro copolymer, wherein the relative amounts of the first moiety and the second moiety are effective to provide the coating and film produced therefrom with properties effective for use in treating implantable medical devices.

The present invention provides polymeric coatings comprising a polyfluoro copolymer and implantable medical devices, for example, stents coated with a film of the polymeric coating in amounts effective to reduce thrombosis and/or restenosis when such stents are used in, for example, angioplasty procedures. As used herein, polyfluoro copolymers means those copolymers comprising an amount of a first moiety selected from the group consisting of polymerized vinylidenefluoride and polymerized tetrafluoroethylene, and an amount of a second moiety other than the first moiety and which is copolymerized with the first moiety to produce the polyfluoro copolymer, the second moiety being capable of providing toughness or elastomeric properties to the polyfluoro copolymer, wherein the relative amounts of the first moiety and the second moiety are effective to provide coatings and film made from such polyfluoro copolymers with properties effective for use in coating implantable medical devices.

The coatings may comprise pharmaceutical or therapeutic agents for reducing restenosis, inflammation and/or thrombosis, and stents coated with such coatings may provide sustained release of the agents. Films prepared from certain polyfluoro copolymer coatings of the present invention provide the physical and mechanical properties required of conventional coated medical devices, even where maximum temperature, to which the device coatings and films are exposed, are limited to relatively low temperatures. This is particularly important when using the coating/film to deliver pharmaceutical/therapeutic agents or drugs that are heat sensitive, or when applying the coating onto temperature-sensitive devices such as catheters. When maximum exposure temperature is not an issue, for example, where heat-stable agents such as itraconazole are incorporated into the coatings, higher melting thermoplastic polyfluoro copolymers may be used and, if very high elongation and adhesion is required, elastomers may be used. If desired or required, the polyfluoro elastomers may be crosslinked by standard methods described in, e.g., *Modern Fluoropolymers*, (J. Shires ed.) John Wiley & Sons, New York, 1997, pp. 77-87.

The present invention comprises polyfluoro copolymers that provide improved biocompatible coatings or vehicles for medical devices. These coatings provide inert biocompatible surfaces to be in contact with body tissue of a mammal, for example, a human, sufficient to reduce restenosis, or thrombosis, or other undesirable reactions. While many reported coatings made from polyfluoro homopolymers are insoluble and/or require high heat, for example, greater than about one hundred twenty-five degrees centigrade, to obtain films with adequate physical and mechanical properties for use on implantable devices, for example, stents, or are not particularly tough or elastomeric, films prepared from the polyfluoro copolymers of the present invention provide adequate adhesion, toughness or elasticity, and resistance to cracking when formed on medical devices. In certain exemplary embodiments, this is the case even where the devices are subjected to relatively low maximum temperatures.

The polyfluoro copolymers used for coatings according to the present invention are preferably film-forming polymers that have molecular weight high enough so as not to be waxy or tacky. The polymers and films formed therefrom should preferably adhere to the stent and not be readily deformable after deposition on the stent as to be able to be displaced by hemodynamic stresses. The polymer molecular weight should preferably be high enough to provide sufficient toughness so that films comprising the polymers will not be rubbed off during handling or deployment of the stent. In certain exemplary embodiments the coating will not crack where expansion of the stent or other medical devices occurs.

Coatings of the present invention comprise polyfluoro copolymers, as defined hereinabove. The second moiety polymerized with the first moiety to prepare the polyfluoro copolymer may be selected from those polymerized, biocompatible monomers that would provide biocompatible polymers acceptable for implantation in a mammal, while maintaining sufficient elastomeric film properties for use on medical devices claimed herein. Such monomers include, without limitation, hexafluoropropylene (HFP), tetrafluoroethylene (TFE), vinylidenefluoride, 1-hydropentafluoropropylene, perfluoro(methyl vinyl ether), chlorotrifluoroethylene (CTFE), pentafluoropropene, trifluoroethylene, hexafluoroacetone and hexafluoroisobutylene.

Polyfluoro copolymers used in the present invention typically comprise vinylidinefluoride copolymerized with hexafluoropropylene, in the weight ratio in the range of from about fifty to about ninety-two weight percent vinylidinefluoride to about fifty to about eight weight percent HFP. Preferably, polyfluoro copolymers used in the present invention comprise from about fifty to about eighty-five weight percent vinylidinefluoride copolymerized with from about fifty to about fifteen weight percent HFP. More preferably, the polyfluoro copolymers will comprise from about fifty-five to about seventy weight percent vinylidineflyoride copolymerized with from about forty-five to about thirty weight percent HFP. Even more preferably, polyfluoro copolymers comprise from about fifty-five to about sixty-five weight percent vinylidinefluoride copolymerized with from about forty-five to about thirty-five weight percent HFP. Such polyfluoro copolymers are soluble, in varying degrees, in solvents such as dimethylacetamide (DMAc), tetrahydrofuran, dimethyl formamide, dimethyl sulfoxide and n-methyl pyrrolidone. Some are soluble in methylethylketone (MEK), acetone, methanol and other solvents commonly used in applying coatings to conventional implantable medical devices.

Conventional polyfluoro homopolymers are crystalline and difficult to apply as high quality films onto metal surfaces without exposing the coatings to relatively high temperatures that correspond to the melting temperature (Tm) of the polymer. The elevated temperature serves to provide films prepared from such PVDF homopolymer coatings that exhibit sufficient adhesion of the film to the device, while preferably maintaining sufficient flexibility to resist film cracking upon expansion/contraction of the coated medical device. Certain films and coatings according to the present invention provide these same physical and mechanical properties, or essentially the same properties, even when the maximum temperatures to which the coatings and films are exposed is less than about a maximum predetermined temperature. This is particularly important when the coatings/films comprise pharmaceutical or therapeutic agents or drugs that are heat sensitive, for example, subject to chemical or physical degradation or other heat-induced negative affects, or when coating heat sensitive substrates of medical devices, for example, subject to heat-induced compositional or structural degradation.

Depending on the particular device upon which the coatings and films of the present invention are to be applied and the particular use/result required of the device, polyfluoro copolymers used to prepare such devices may be crystalline, semi-crystalline or amorphous.

Where devices have no restrictions or limitations with respect to exposure of same to elevated temperatures, crystalline polyfluoro copolymers may be employed. Crystalline polyfluoro copolymers tend to resist the tendency to flow under applied stress or gravity when exposed to temperatures above their glass transition (Tg) temperatures. Crystalline polyfluoro copolymers provide tougher coatings and films than their fully amorphous counterparts. In addition, crystalline polymers are more lubricious and more easily handled through crimping and transfer processes used to mount self-expanding stents, for example, nitinol stents.

Semi-crystalline and amorphous polyfluoro copolymers are advantageous where exposure to elevated temperatures is an issue, for example, where heat-sensitive pharmaceutical or therapeutic agents are incorporated into the coatings and films, or where device design, structure and/or use preclude exposure to such elevated temperatures. Semi-crystalline polyfluoro copolymer elastomers comprising relatively high levels, for example, from about thirty to about forty-five weight percent of the second moiety, for example, HFP, copolymerized with the first moiety, for example, VDF, have the advantage of reduced coefficient of friction and self-blocking relative to amorphous polyfluoro copolymer elastomers. Such characteristics may be of significant value when processing, packaging and delivering medical devices coated with such polyfluoro copolymers. In addition, such polyfluoro copolymer elastomers comprising such relatively high content of the second moiety serves to control the solubility of certain agents, for example, rapamycin, in the polymer and therefore controls permeability of the agent through the matrix.

Polyfluoro copolymers utilized in the present inventions may be prepared by various known polymerization methods. For example, high pressure, free-radical, semi-continuous emulsion polymerization techniques such as those disclosed in *Fluoroelastomers—dependence of relaxation phenomena on compositions*, POLYMER 30, 2180, 1989, by Ajroldi, et al., may be employed to prepare amorphous polyfluoro copolymers, some of which may be elastomers. In addition, free-radical batch emulsion polymerization techniques disclosed herein may be used to obtain polymers that are semi-crystalline, even where relatively high levels of the second moiety are included.

As described above, stents may comprise a wide variety of materials and a wide variety of geometrics. Stents may be made of biocomptible materials, including biostable and bioabsorbable materials. Suitable biocompatible metals include, but are not limited to, stainless steel, tantalum, titanium alloys (including nitinol), and cobalt alloys (including cobalt-chromium nickel alloys). Suitable nonmetallic biocompatible materials include, but are not limited to, polyamides, polyolefins (i.e. polypropylene, polyethylene etc.), nonabsorbable polyesters (i.e. polyethylene terephthalate), and bioabsorbable aliphatic polyesters (i.e. homopolymers and copolymers of lactic acid, glycolic acid, lactide, glycolide, para-dioxanone, trimethylene carbonate, ϵ-caprolactone, and blends thereof).

The film-forming biocompatible polymer coatings generally are applied to the stent in order to reduce local turbulence in blood flow through the stent, as well as adverse tissue reactions. The coatings and films formed therefrom also may be used to administer a pharmaceutically active material to

the site of the stent placement. Generally, the amount of polymer coating to be applied to the stent will vary depending on, among other possible parameters, the particular polyfluoro copolymer used to prepare the coating, the stent design and the desired effect of the coating. Generally, the coated stent will comprise from about 0.1 to about fifteen weight percent of the coating, preferably from about 0.4 to about ten weight percent. The polyfluoro copolymer coatings may be applied in one or more coating steps, depending on the amount of polyfluoro copolymer to be applied. Different polyfluoro copolymers may be used for different layers in the stent coating. In fact, in certain exemplary embodiments, it is highly advantageous to use a diluted first coating solution comprising a polyfluoro copolymer as a primer to promote adhesion of a subsequent polyfluoro copolymer coating layer that may include pharmaceutically active materials. The individual coatings may be prepared from different polyfluoro copolymers.

Additionally, a top coating may be applied to delay release of the pharmaceutical agent, or they could be used as the matrix for the delivery of a different pharmaceutically active material. Layering of coatings may be used to stage release of the drug or to control release of different agents placed in different layers.

Blends of polyfluoro copolymers may also be used to control the release rate of different agents or to provide a desirable balance of coating properties, i.e. elasticity, toughness, etc., and drug delivery characteristics, for example, release profile. Polyfluoro copolymers with different solubilities in solvents may be used to build up different polymer layers that may be used to deliver different drugs or to control the release profile of a drug. For example, polyfluoro copolymers comprising 85.5/14.5 (wt/wt) of poly(vinylidinefluoride/HFP) and 60.6/39.4 (wt/wt) of poly(vinylidinefluoride/HFP) are both soluble in DMAc. However, only the 60.6/39.4 PVDF polyfluoro copolymer is soluble in methanol. So, a first layer of the 85.5/14.5 PVDF polyfluoro copolymer comprising a drug could be over coated with a topcoat of the 60.6/39.4 PVDF polyfluoro copolymer made with the methanol solvent. The top coating may be used to delay the drug delivery of the drug contained in the first layer. Alternately, the second layer could comprise a different drug to provide for sequential drug delivery. Multiple layers of different drugs could be provided by alternating layers of first one polyfluoro copolymer, then the other. As will be readily appreciated by those skilled in the art, numerous layering approaches may be used to provide the desired drug delivery.

Coatings may be formulated by mixing one or more therapeutic agents with the coating polyfluoro copolymers in a coating mixture. The therapeutic agent may be present as a liquid, a finely divided solid, or any other appropriate physical form. Optionally, the coating mixture may include one or more additives, for example, nontoxic auxiliary substances such as diluents, carriers, excipients, stabilizers or the like. Other suitable additives may be formulated with the polymer and pharmaceutically active agent or compound. For example, a hydrophilic polymer may be added to a biocompatible hydrophobic coating to modify the release profile, or a hydrophobic polymer may be added to a hydrophilic coating to modify the release profile. One example would be adding a hydrophilic polymer selected from the group consisting of polyethylene oxide, polyvinyl pyrrolidone, polyethylene glycol, carboxylmethyl cellulose, and hydroxymethyl cellulose to a polyfluoro copolymer coating to modify the release profile. Appropriate relative amounts may be determined by monitoring the in vitro and/or in vivo release profiles for the therapeutic agents.

The best conditions for the coating application are when the polyfluoro copolymer and pharmaceutic agent have a common solvent. This provides a wet coating that is a true solution. Less desirable, yet still usable, are coatings that contain the pharmaceutical agent as a solid dispersion in a solution of the polymer in solvent. Under the dispersion conditions, care must be taken to ensure that the particle size of the dispersed pharmaceutical powder, both the primary powder size and its aggregates and agglomerates, is small enough not to cause an irregular coating surface or to clog the slots of the stent that need to remain essentially free of coating. In cases where a dispersion is applied to the stent and the smoothness of the coating film surface requires improvement, or to be ensured that all particles of the drug are fully encapsulated in the polymer, or in cases where the release rate of the drug is to be slowed, a clear (polyfluoro copolymer only) topcoat of the same polyfluoro copolymer used to provide sustained release of the drug or another polyfluoro copolymer that further restricts the diffusion of the drug out of the coating may be applied. The topcoat may be applied by dip coating with mandrel to clear the slots. This method is disclosed in U.S. Pat. No. 6,153,252. Other methods for applying the topcoat include spin coating and spray coating. Dip coating of the topcoat can be problematic if the drug is very soluble in the coating solvent, which swells the polyfluoro copolymer, and the clear coating solution acts as a zero concentration sink and redissolves previously deposited drug. The time spent in the dip bath may need to be limited so that the drug is not extracted out into the drug-free bath. Drying should be rapid so that the previously deposited drug does not completely diffuse into the topcoat.

The amount of therapeutic agent will be dependent upon the particular drug employed and medical condition being treated. Typically, the amount of drug represents about 0.001 percent to about seventy percent, more typically about 0.001 percent to about sixty percent.

The quantity and type of polyfluoro copolymers employed in the coating film comprising the pharmaceutic agent will vary depending on the release profile desired and the amount of drug employed. The product may contain blends of the same or different polyfluoro copolymers having different molecular weights to provide the desired release profile or consistency to a given formulation.

Polyfluoro copolymers may release dispersed drug by diffusion. This can result in prolonged delivery (over, say approximately one to two-thousand hours, preferably two to eight-hundred hours) of effective amounts (0.001 $\mu g/cm^2$-min to 1000 $\mu g/cm^2$-min) of the drug. The dosage may be tailored to the subject being treated, the severity of the affliction, the judgment of the prescribing physician, and the like.

Individual formulations of drugs and polyfluoro copolymers may be tested in appropriate in vitro and in vivo models to achieve the desired drug release profiles. For example, a drug could be formulated with a polyfluoro copolymer, or blend of polyfluoro copolymers, coated onto a stent and placed in an agitated or circulating fluid system, for example, twenty-five percent ethanol in water. Samples of the circulating fluid could be taken to determine the release profile (such as by HPLC, UV analysis or use of radiotagged molecules). The release of a pharmaceutical compound from a stent coating into the interior wall of a lumen could be modeled in appropriate animal system. The drug release profile could then be monitored by appropriate means such as, by taking samples at specific times and assaying the samples for drug concentration (using HPLC to detect drug concentration). Thrombus formation can be modeled in animal models using the In-platelet imaging methods described by Hanson and

Harker, Proc. Natl. Acad. Sci. USA 85:3184-3188 (1988). Following this or similar procedures, those skilled in the art will be able to formulate a variety of stent coating formulations.

While not a requirement of the present invention, the coatings and films may be crosslinked once applied to the medical devices. Crosslinking may be affected by any of the known crosslinking mechanisms, such as chemical, heat or light. In addition, crosslinking initiators and promoters may be used where applicable and appropriate. In those exemplary embodiments utilizing crosslinked films comprising pharmaceutical agents, curing may affect the rate at which the drug diffuses from the coating. Crosslinked polyfluoro copolymers films and coatings of the present invention also may be used without drug to modify the surface of implantable medical devices.

EXAMPLES

Example 1

A PVDF homopolymer (Solef® 1008 from Solvay Advanced Polymers, Houston, Tex., Tm about 175° C.) and polyfluoro copolymers of poly(vinylidenefluoride/HFP), 92/8 and 91/9 weight percent vinylidenefluoride/HFP as determined by F^{19} NMR, respectively (eg: Solef® 11010 and 11008, Solvay Advanced Polymers, Houston, Tex., Tm about 159 degrees C. and 160 degrees C., respectively) were examined as potential coatings for stents. These polymers are soluble in solvents such as, but not limited to, DMAc, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), N-methylpyrrolidone (NMP), tetrahydrofuran (THF) and acetone. Polymer coatings were prepared by dissolving the polymers in acetone, at five weight percent as a primer, or by dissolving the polymer in 50/50 DMAc/acetone, at thirty weight percent as a topcoat. Coatings that were applied to the stents by dipping and dried at 60 degrees C. in air for several hours, followed by 60 degrees C. for three hours in a <100 mm Hg vacuum, resulted in white foamy films. As applied, these films adhered poorly to the stent and flaked off, indicating they were too brittle. When stents coated in this manner were heated above 175 degrees C., i.e. above the melting temperature of the polymer, a clear, adherent film was formed. Since coatings require high temperatures, for example, above the melting temperature of the polymer, to achieve high quality films. As mentioned above, the high temperature heat treatment is unacceptable for the majority of drug compounds due to their thermal sensitivity.

Example 2

A polyfluoro copolymer (Solef® 21508) comprising 85.5 weight percent vinylidenefluoride copolymerized with 14.5 weight percent HFP, as determined by F^{19} NMR, was evaluated. This copolymer is less crystalline than the polyfluoro homopolymer and copolymers described in Example 1. It also has a lower melting point reported to be about 133 degrees C. Once again, a coating comprising about twenty weight percent of the polyfluoro copolymer was applied from a polymer solution in 50/50 DMAc/MEK. After drying (in air) at 60 degrees C. for several hours, followed by 60 degrees C. for three hours in a <100 mtorr Hg vacuum, clear adherent films were obtained. This eliminated the need for a high temperature heat treatment to achieve high quality films. Coatings were smoother and more adherent than those of Example 1. Some coated stents that underwent expansion show some degree of adhesion loss and "tenting" as the film pulls away from the metal. Where necessary, modification of coatings containing such copolymers may be made, e.g. by addition of plasticizers or the like to the coating compositions. Films prepared from such coatings may be used to coat stents or other medical devices, particularly where those devices are not susceptible to expansion to the degree of the stents.

The coating process above was repeated, this time with a coating comprising the 85.5/14.6 (wt/wt) (vinylidenefluoride/HFP) and about thirty weight percent of rapamycin (Wyeth-Ayerst Laboratories, Philadelphia, Pa.), based on total weight of coating solids. Clear films that would occasionally crack or peel upon expansion of the coated stents resulted. It is believed that inclusion of plasticizers and the like in the coating composition will result in coatings and films for use on stents and other medical devices that are not susceptible to such cracking and peeling.

Example 3

Polyfluoro copolymers of still higher HFP content were then examined. This series of polymers were not semicrystalline, but rather are marketed as elastomers. One such copolymer is Fluorel™ FC2261Q (from Dyneon, a 3M-Hoechst Enterprise, Oakdale, Minn.), a 60.6/39.4 (wt/wt) copolymer of vinylidenefluoride/HFP. Although this copolymer has a Tg well below room temperature (Tg about minus twenty degrees C.) it is not tacky at room temperature or even at sixty degrees C. This polymer has no detectable crystallinity when measured by Differential Scanning Calorimetry (DSC) or by wide angle X-ray diffraction. Films formed on stents as described above were non-tacky, clear, and expanded without incident when the stents were expanded.

The coating process above was repeated, this time with coatings comprising the 60.6/39.4 (wt/wt) (vinylidenefluoride/HFP) and about nine, thirty and fifty weight percent of rapamycin (Wyeth-Ayerst Laboratories, Philadelphia, Pa.), based on total weight of coating solids, respectively. Coatings comprising about nine and thirty weight percent rapamycin provided white, adherent, tough films that expanded without incident on the stent. Inclusion of fifty percent drug, in the same manner, resulted in some loss of adhesion upon expansion.

Changes in the comonomer composition of the polyfluoro copolymer also can affect the nature of the solid state coating, once dried. For example, the semicrystalline copolymer, Solef® 21508, containing 85.5 percent vinylidenefluoride polymerized with 14.5 percent by weight HFP forms homogeneous solutions with about 30 percent rapamycin (drug weight divided by total solids weight, for example, drug plus copolymer) in DMAc and 50/50 DMAc/MEK. When the film is dried (60 degrees C./16 hours followed by 60 degrees C./3 hours in vacuum of 100 mm Hg) a clear coating, indicating a solid solution of the drug in the polymer, is obtained. Conversely, when an amorphous copolymer, Fluorel™ FC2261Q, of PDVF/HFP at 60.6/39.5 (wt/wt) forms a similar thirty percent solution of rapamycin in DMAc/MEK and is similarly dried, a white film, indicating phase separation of the drug and the polymer, is obtained. This second drug containing film is much slower to release the drug into an in vitro test solution of twenty-five percent ethanol in water than is the former clear film of crystalline Solef® 21508. X-ray analysis of both films indicates that the drug is present in a non-crystalline form. Poor or very low solubility of the drug in the high HFP containing copolymer results in slow permeation of the drug through the thin coating film. Permeability is

the product of diffusion rate of the diffusing species (in this case the drug) through the film (the copolymer) and the solubility of the drug in the film.

Example 4

In Vitro Release Results of Rapamycin from Coating

FIG. 3 is a plot of data for the 85.5/14.5 vinylidenefluoride/HFP polyfluoro copolymer, indicating fraction of drug released as a function of time, with no topcoat. FIG. 4 is a plot of data for the same polyfluoro copolymer over which a topcoat has been disposed, indicating that most effect on release rate is with a clear topcoat. As shown therein, TC150 refers to a device comprising one hundred fifty micrograms of topcoat, TC235 refers to two hundred thirty-five micrograms of topcoat, etc. The stents before topcoating had an average of seven hundred fifty micrograms of coating containing thirty percent rapamycin. FIG. 5 is a plot for the 60.6/39.4 vinylidenefluoride/HFP polyfluoro copolymer, indicating fraction of drug released as a function of time, showing significant control of release rate from the coating without the use of a topcoat. Release is controlled by loading of drug in the film.

Example 5

In Vivo Stent Release Kinetics of Rapamycin from Poly(VDF/HFP)

Nine New Zealand white rabbits (2.5-3.0 kg) on a normal diet were given aspirin twenty-four hours prior to surgery, again just prior to surgery and for the remainder of the study. At the time of surgery, animals were premedicated with Acepromazine (0.1-0.2 mg/kg) and anesthetized with a Ketamine/Xylazine mixture (40 mg/kg and 5 mg/kg, respectively). Animals were given a single intraprocedural dose of heparin (150 IU/kg, i.v.)

Arteriectomy of the right common carotid artery was performed and a 5 F catheter introducer (Cordis, Inc.) placed in the vessel and anchored with ligatures. Iodine contrast agent was injected to visualize the right common carotid artery, brachlocephalic trunk and aortic arch. A steerable guide wire (0.014 inch/180 cm, Cordis, Inc.) was inserted via the introducer and advanced sequentially into each iliac artery to a location where the artery possesses a diameter closest to 2 mm using the angiographic mapping done previously. Two stents coated with a film made of poly(VDF/HFP): (60.6/39.4) with thirty percent rapamycin were deployed in each animal where feasible, one in each iliac artery, using 3.0 mm balloon and inflation to 8-10 ATM for thirty seconds followed after a one minute interval by a second inflation to 8-10 ATM for thirty seconds. Follow-up angiographs visualizing both iliac arteries are obtained to confirm correct deployment position of the stent.

At the end of procedure, the carotid artery was ligated and the skin is closed with 3/0 vicryl suture using a one layered interrupted closure. Animals were given butoropanol (0.4 mg/kg, s.c.) and gentamycin (4 mg/kg, i.m.). Following recovery, the animals were returned to their cages and allowed free access to food and water.

Due to early deaths and surgical difficulties, two animals were not used in this analysis. Stented vessels were removed from the remaining seven animals at the following time points: one vessel (one animal) at ten minutes post implant; six vessels (three animals) between forty minutes and two hours post-implant (average, 1.2 hours); two vessels (two animals) at three days post implant; and two vessels (one animal) at seven days post-implant. In one animal at two hours, the stent was retrieved from the aorta rather than the iliac artery. Upon removal, arteries were carefully trimmed at both the proximal and distal ends of the stent. Vessels were then carefully dissected free of the stent, flushed to remove any residual blood, and both stent and vessel frozen immediately, wrapped separately in foil, labeled and kept frozen at minus eighty degrees C. When all samples had been collected, vessels and stents were frozen, transported and subsequently analyzed for rapamycin in tissue and results are illustrated in FIG. 4.

Example 6

Purifying the Polymer

The Fluorel™ FC2261Q copolymer was dissolved in MEK at about ten weight percent and was washed in a 50/50 mixture of ethanol/water at a 14:1 of ethanol/water to the MEK solution ratio. The polymer precipitated out and was separated from the solvent phase by centrifugation. The polymer again was dissolved in MEK and the washing procedure repeated. The polymer was dried after each washing step at sixty degrees C. in a vacuum oven (<200 mtorr) over night.

Example 7

In Vivo Testing of Coated Stents in Porcine Coronary Arteries

CrossFlex® stents (available from Cordis, a Johnson & Johnson Company) were coated with the "as received" Fluorel™ FC2261Q PVDF copolymer and with the purified polyfluoro copolymer of Example 6, using the dip and wipe approach. The coated stents were sterilized using ethylene oxide and a standard cycle. The coated stents and bare metal stents (controls) were implanted in porcine coronary arteries, where they remained for twenty-eight days.

Angiography was performed on the pigs at implantation and at twenty-eight days. Angiography indicated that the control uncoated stent exhibited about twenty-one percent restenosis. The polyfluoro copolymer "as received" exhibited about twenty-six percent restenosis (equivalent to the control) and the washed copolymer exhibited about 12.5 percent restenosis.

Histology results reported neointimal area at twenty-eight days to be 2.89±0.2, 3.57±0.4 and 2.75±0.3, respectively, for the bare metal control, the unpurified copolymer and the purified copolymer.

Since rapamycin acts by entering the surrounding tissue, it is preferably only affixed to the surface of the stent making contact with one tissue. Typically, only the outer surface of the stent makes contact with the tissue. Accordingly, in one exemplary embodiment, only the outer surface of the stent is coated with rapamycin.

The circulatory system, under normal conditions, has to be self-sealing, otherwise continued blood loss from an injury would be life threatening. Typically, all but the most catastrophic bleeding is rapidly stopped though a process known as hemostasis. Hemostasis occurs through a progression of steps. At high rates of flow, hemostasis is a combination of events involving platelet aggregation and fibrin formation. Platelet aggregation leads to a reduction in the blood flow due to the formation of a cellular plug while a cascade of biochemical steps leads to the formation of a fibrin clot.

Fibrin clots, as stated above, form in response to injury. There are certain circumstances where blood clotting or clotting in a specific area may pose a health risk. For example, during percutaneous transluminal coronary angioplasty, the endothelial cells of the arterial walls are typically injured, thereby exposing the sub-endothelial cells. Platelets adhere to these exposed cells. The aggregating platelets and the damaged tissue initiate further biochemical process resulting in blood coagulation. Platelet and fibrin blood clots may prevent the normal flow of blood to critical areas. Accordingly, there is a need to control blood clotting in various medical procedures. Compounds that do not allow blood to clot are called anti-coagulants. Essentially, an anti-coagulant is an inhibitor of thrombin formation or function. These compounds include drugs such as heparin and hirudin. As used herein, heparin includes all direct or indirect inhibitors of thrombin or Factor Xa.

In addition to being an effective anti-coagulant, heparin has also been demonstrated to inhibit smooth muscle cell growth in vivo. Thus, heparin may be effectively utilized in conjunction with rapamycin in the treatment of vascular disease. Essentially, the combination of rapamycin and heparin may inhibit smooth muscle cell growth via two different mechanisms in addition to the heparin acting as an anti-coagulant.

Because of its multifunctional chemistry, heparin may be immobilized or affixed to a stent in a number of ways. For example, heparin may be immobilized onto a variety of surfaces by various methods, including the photolink methods set forth in U.S. Pat. Nos. 3,959,078 and 4,722,906 to Guire et al. and U.S. Pat. Nos. 5,229,172; 5,308,641; 5,350,800 and 5,415,938 to Cahalan et al. Heparinized surfaces have also been achieved by controlled release from a polymer matrix, for example, silicone rubber, as set forth in U.S. Pat. Nos. 5,837,313; 6,099,562 and 6,120,536 to Ding et al.

In one exemplary embodiment, heparin may be immobilized onto the stent as briefly described below. The surface onto which the heparin is to be affixed is cleaned with ammonium peroxidisulfate. Once cleaned, alternating layers of polyethylenimine and dextran sulfate are deposited thereon. Preferably, four layers of the polyethylenimine and dextran sulfate are deposited with a final layer of polyethylenimine. Aldehyde-end terminated heparin is then immobilized to this final layer and stabilized with sodium cyanoborohydride. This process is set forth in U.S. Pat. Nos. 4,613,665; 4,810,784 to Larm and U.S. Pat. No. 5,049,403 to Larm et al.

Unlike rapamycin, heparin acts on circulating proteins in the blood and heparin need only make contact with blood to be effective. Accordingly, if used in conjunction with a medical device, such as a stent, it would preferably be only on the side that comes into contact with the blood. For example, if heparin were to be administered via a stent, it would only have to be on the inner surface of the stent to be effective.

In an exemplary embodiment of the invention, a stent may be utilized in combination with rapamycin and heparin to treat vascular disease. In this exemplary embodiment, the heparin is immobilized to the inner surface of the stent so that it is in contact with the blood and the rapamycin is immobilized to the outer surface of the stent so that it is in contact with the surrounding tissue. FIG. **7** illustrates a cross-section of a band **102** of the stent **100** illustrated in FIG. **1**. As illustrated, the band **102** is coated with heparin **108** on its inner surface **110** and with rapamycin **112** on its outer surface **114**.

In an alternate exemplary embodiment, the stent may comprise a heparin layer immobilized on its inner surface, and rapamycin and heparin on its outer surface. Utilizing current coating techniques, heparin tends to form a stronger bond with the surface it is immobilized to then does rapamycin. Accordingly, it may be possible to first immobilize the rapamycin to the outer surface of the stent and then immobilize a layer of heparin to the rapamycin layer. In this embodiment, the rapamycin may be more securely affixed to the stent while still effectively eluting from its polymeric matrix, through the heparin and into the surrounding tissue. FIG. **8** illustrates a cross-section of a band **102** of the stent **100** illustrated in FIG. **1**. As illustrated, the band **102** is coated with heparin **108** on its inner surface **110** and with rapamycin **112** and heparin **108** on its outer surface **114**.

There are a number of possible ways to immobilize, i.e., entrapment or covalent linkage with an erodible bond, the heparin layer to the rapamycin layer. For example, heparin may be introduced into the top layer of the polymeric matrix. In other embodiments, different forms of heparin may be directly immobilized onto the top coat of the polymeric matrix, for example, as illustrated in FIG. **9**. As illustrated, a hydrophobic heparin layer **116** may be immobilized onto the top coat layer **118** of the rapamycin layer **112**. A hydrophobic form of heparin is utilized because rapamycin and heparin coatings represent incompatible coating application technologies. Rapamycin is an organic solvent-based coating and heparin, in its native form, is a water-based coating.

As stated above, a rapamycin coating may be applied to stents by a dip, spray or spin coating method, and/or any combination of these methods. Various polymers may be utilized. For example, as described above, poly(ethylene-co-vinyl acetate) and polybutyl methacrylate blends may be utilized. Other polymers may also be utilized, but not limited to, for example, polyvinylidene fluoride-co-hexafluoropropylene and polyethylbutyl methacrylate-co-hexyl methacrylate. Also as described above, barrier or top coatings may also be applied to modulate the dissolution of rapamycin from the polymer matrix. In the exemplary embodiment described above, a thin layer of heparin is applied to the surface of the polymeric matrix. Because these polymer systems are hydrophobic and incompatible with the hydrophilic heparin, appropriate surface modifications may be required.

The application of heparin to the surface of the polymeric matrix may be performed in various ways and utilizing various biocompatible materials. For example, in one embodiment, in water or alcoholic solutions, polyethylene imine may be applied on the stents, with care not to degrade the rapamycin (e.g., pH<7, low temperature), followed by the application of sodium heparinate in aqueous or alcoholic solutions. As an extension of this surface modification, covalent heparin may be linked on polyethylene imine using amide-type chemistry (using a carbondiimide activator, e.g. EDC) or reductive amination chemistry (using CBAS-heparin and sodium cyanoborohydride for coupling). In another exemplary embodiment, heparin may be photolinked on the surface, if it is appropriately grafted with photo initiator moieties. Upon application of this modified heparin formulation on the covalent stent surface, light exposure causes cross-linking and immobilization of the heparin on the coating surface. In yet another exemplary embodiment, heparin may be complexed with hydrophobic quaternary ammonium salts, rendering the molecule soluble in organic solvents (e.g. benzalkonium heparinate, troidodecylmethylammonium heparinate). Such a formulation of heparin may be compatible with the hydrophobic rapamycin coating, and may be applied directly on the coating surface, or in the rapamycin/hydrophobic polymer formulation.

It is important to note that the stent, as described above, may be formed from any number of materials, including various metals, polymeric materials and ceramic materials. Accordingly, various technologies may be utilized to immo-

bilize the various drugs, agent, compound combinations thereon. Specifically, in addition to the polymeric matricies, described above, biopolymers may be utilized. Biopolymers may be generally classified as natural polymers, while the above-described polymers may be described as synthetic polymers. Exemplary biopolymers, which may be utilized include agarose, alginate, gelatin, collagen and elastin. In addition, the drugs, agents or compounds may be utilized in conjunction with other percutaneously delivered medical devices such as grafts and perfusion balloons.

In addition to utilizing an anti-proliferative and anti-coagulant, anti-inflammatories may also be utilized in combination therewith. One example of such a combination would be the addition of an anti-inflammatory corticosteroid such as dexamethasone with an anti-proliferative, such as rapamycin, cladribine, vincristine, taxol, or a nitric oxide donor and an anti-coagulant, such as heparin. Such combination therapies might result in a better therapeutic effect, i.e., less proliferation as well as less inflammation, a stimulus for proliferation, than would occur with either agent alone. The delivery of a stent comprising an anti-proliferative, anti-coagulant, and an anti-inflammatory to an injured vessel would provide the added therapeutic benefit of limiting the degree of local smooth muscle cell proliferation, reducing a stimulus for proliferation, i.e., inflammation and reducing the effects of coagulation thus enhancing the restenosis-limiting action of the stent.

In other exemplary embodiments of the inventions, growth factor inhibitor or cytokine signal transduction inhibitor, such as the ras inhibitor, R115777 or P38 kinase inhibitor RWJ67657, or a tyrosine kinase inhibitor, such as tyrphostin, might be combined with an anti-proliferative agent such as taxol, vincristine or rapamycin so that proliferation of smooth muscle cells could be inhibited by different mechanisms. Alternatively, an anti-proliferative agent such as taxol, vincristine or rapamycin could be combined with an inhibitor of extracellular matrix synthesis such as halofuginone. In the above cases, agents acting by different mechanisms could act synergistically to reduce smooth muscle cell proliferation and vascular hyperplasia. This invention is also intended to cover other combinations of two or more such drug agents. As mentioned above, such drugs, agents or compounds could be administered systemically, delivered locally via drug delivery catheter, or formulated for delivery from the surface of a stent, or given as a combination of systemic and local therapy.

In addition to anti-proliferatives, anti-inflammatories and anti-coagulants, other drugs, agents or compounds may be utilized in conjunction with the medical devices. For example, immunosuppressants may be utilized alone or in combination with these other drugs, agents or compounds. Also gene therapy delivery mechanisms such as modified genes (nucleic acids including recombinant DNA) in viral vectors and non-viral gene vectors such as plasmids may also be introduced locally via a medical device. In addition, the present invention may be utilized with cell based therapy.

In addition to all of the drugs, agents, compounds and modified genes described above, chemical agents that are not ordinarily therapeutically or biologically active may also be utilized in conjunction with the present invention. These chemical agents, commonly referred to as pro-drugs, are agents that become biologically active upon their introduction into the living organism by one or more mechanisms. These mechanisms include the addition of compounds supplied by the organism or the cleavage of compounds from the agents caused by another agent supplied by the organism. Typically, pro-drugs are more absorbable by the organism. In addition, pro-drugs may also provide some additional measure of time release.

The coatings and drugs, agents or compounds described above may be utilized in combination with any number of medical devices, and in particular, with implantable medical devices such as stents and stent-grafts. Other devices such as vena cava filters and anastomosis devices may be used with coatings having drugs, agents or compounds therein. The exemplary stent illustrated in FIGS. **1** and **2** is a balloon expandable stent. Balloon expandable stents may be utilized in any number of vessels or conduits, and are particularly well suited for use in coronary arteries. Self-expanding stents, on the other hand, are particularly well suited for use in vessels where crush recovery is a critical factor, for example, in the carotid artery. Accordingly, it is important to note that any of the drugs, agents or compounds, as well as the coatings described above, may be utilized in combination with self-expanding stents such as those described below.

There is illustrated in FIGS. **10** and **11**, a stent **200**, which may be utilized in connection with the present invention. FIGS. **10** and **11** illustrate the exemplary stent **200** in its unexpanded or compressed state. The stent **200** is preferably made from a superelastic alloy such as Nitinol. Most preferably, the stent **200** is made from an alloy comprising from about fifty percent (as used herein these percentages refer to weight percentages) Ni to about sixty percent Ni, and more preferably about 55.8 percent Ni, with the remainder of the alloy being Ti. Preferably, the stent **200** is designed such that it is superelastic at body temperature, and preferably has an Af in the range from about twenty-four degrees C. to about thirty-seven degrees C. The superelastic design of the stent **200** makes it crush recoverable which, as discussed above, makes it useful as a stent or frame for any number of vascular devices in different applications.

Stent **200** is a tubular member having front and back open ends **202** and **204** and a longitudinal axis **206** extending therebetween. The tubular member has a first smaller diameter, FIGS. **10** and **11**, for insertion into a patient and navigation through the vessels, and a second larger diameter, FIGS. **12** and **13**, for deployment into the target area of a vessel. The tubular member is made from a plurality of adjacent hoops **208**, FIG. **10** showing hoops **208**(*a*)-**208**(*d*), extending between the front and back ends **202** and **204**. The hoops **208** include a plurality of longitudinal struts **210** and a plurality of loops **212** connecting adjacent struts, wherein adjacent struts are connected at opposite ends so as to form a substantially S or Z shape pattern. The loops **212** are curved, substantially semi-circular with symmetrical sections about their centers **214**.

Stent **200** further includes a plurality of bridges **216** which connect adjacent hoops **208** and which can best be described in detail by referring to FIG. **14**. Each bridge **216** has two ends **218** and **220**. The bridges **216** have one end attached to one strut and/or loop, and another end attached to a strut and/or loop on an adjacent hoop. The bridges **216** connect adjacent struts together at bridge to loop connection points **222** and **224**. For example, bridge end **218** is connected to loop **214**(*a*) at bridge to loop connection point **222**, and bridge end **220** is connected to loop **214**(*b*) at bridge to loop connection point **224**. Each bridge to loop connection point has a center **226**. The bridge to loop connection points are separated angularly with respect to the longitudinal axis. That is, the connection points are not immediately opposite each other. Essentially, one could not draw a straight line between the connection points, wherein such line would be parallel to the longitudinal axis of the stent.

The above described geometry helps to better distribute strain throughout the stent, prevents metal to metal contact when the stent is bent, and minimizes the opening size between the struts, loops and bridges. The number of and nature of the design of the struts, loops and bridges are important factors when determining the working properties and fatigue life properties of the stent. It was previously thought that in order to improve the rigidity of the stent, that struts should be large, and therefore there should be fewer struts per hoop. However, it has now been discovered that stents having smaller struts and more struts per hoop actually improve the construction of the stent and provide greater rigidity. Preferably, each hoop has between twenty-four to thirty-six or more struts. It has been determined that a stent having a ratio of number of struts per hoop to strut length L (in inches) which is greater than four hundred has increased rigidity over prior art stents, which typically have a ratio of under two hundred. The length of a strut is measured in its compressed state parallel to the longitudinal axis **206** of the stent **200** as illustrated in FIG. **10**.

As seen from a comparison of FIGS. **10** and **12**, the geometry of the stent **200** changes quite significantly as the stent **200** is deployed from its un-expanded state to its expanded state. As a stent undergoes diametric change, the strut angle and strain levels in the loops and bridges are affected. Preferably, all of the stent features will strain in a predictable manor so that the stent is reliable and uniform in strength. In addition, it is preferable to minimize the maximum strain experienced by struts loops and bridges, since Nitinol properties are more generally limited by strain rather than by stress. As will be discussed in greater detail below, the stent sits in the delivery system in its un-expanded state as shown in FIGS. **19** and **20**. As the stent is deployed, it is allowed to expand towards its expanded state, as shown in FIG. **12**, which preferably has a diameter which is the same or larger than the diameter of the target vessel. Nitinol stents made from wire deploy in much the same manner, and are dependent upon the same design constraints, as laser cut stents. Stainless steel stents deploy similarly in terms of geometric changes as they are assisted by forces from balloons or other devices.

In trying to minimize the maximum strain experienced by features of the stent, the present invention utilizes structural geometries which distribute strain to areas of the stent which are less susceptible to failure than others. For example, one of the most vulnerable areas of the stent is the inside radius of the connecting loops. The connecting loops undergo the most deformation of all the stent features. The inside radius of the loop would normally be the area with the highest level of strain on the stent. This area is also critical in that it is usually the smallest radius on the stent. Stress concentrations are generally controlled or minimized by maintaining the largest radii possible. Similarly, we want to minimize local strain concentrations on the bridge and bridge connection points. One way to accomplish this is to utilize the largest possible radii while maintaining feature widths which are consistent with applied forces. Another consideration is to minimize the maximum open area of the stent. Efficient utilization of the original tube from which the stent is cut increases stent strength and its ability to trap embolic material.

Many of these design objectives have been accomplished by an exemplary embodiment of the present invention, illustrated in FIGS. **10**, **11** and **14**. As seen from these figures, the most compact designs which maintain the largest radii at the loop to bridge connections are non-symmetric with respect to the centerline of the strut connecting loop. That is, loop to bridge connection point centers **226** are offset from the center **214** of the loops **212** to which they are attached. This feature is particularly advantageous for stents having large expansion ratios, which in turn requires them to have extreme bending requirements where large elastic strains are required. Nitinol can withstand extremely large amounts of elastic strain deformation, so the above features are well suited to stents made from this alloy. This feature allows for maximum utilization of Ni—Ti or other material properties to enhance radial strength, to improve stent strength uniformity, to improve fatigue life by minimizing local strain levels, to allow for smaller open areas which enhance entrapment of embolic material, and to improve stent apposition in irregular vessel wall shapes and curves.

As seen in FIG. **14**, stent **200** comprises strut connecting loops **212** having a width **W1**, as measured at the center **214** parallel to axis **206**, which are greater than the strut widths **W2**, as measured perpendicular to axis **206** itself. In fact, it is preferable that the thickness of the loops vary so that they are thickest near their centers. This increases strain deformation at the strut and reduces the maximum strain levels at the extreme radii of the loop. This reduces the risk of stent failure and allows one to maximize radial strength properties. This feature is particularly advantageous for stents having large expansion ratios, which in turn requires them to have extreme bending requirements where large elastic strains are required. Nitinol can withstand extremely large amounts of elastic strain deformation, so the above features are well suited to stents made from this alloy. As stated above, this feature allows for maximum utilization of Ni—Ti or other material properties to enhance radial strength, to improve stent strength uniformity, to improve fatigue life by minimizing local strain levels, to allow for smaller open areas which enhance entrapment of embolic material, and to improve stent apposition in irregular vessel wall shapes and curves.

As mentioned above, bridge geometry changes as a stent is deployed from its compressed state to its expanded state and vise-versa. As a stent undergoes diametric change, strut angle and loop strain is affected. Since the bridges are connected to either the loops, struts or both, they are affected. Twisting of one end of the stent with respect to the other, while loaded in the stent delivery system, should be avoided. Local torque delivered to the bridge ends displaces the bridge geometry. If the bridge design is duplicated around the stent perimeter, this displacement causes rotational shifting of the two loops being connected by the bridges. If the bridge design is duplicated throughout the stent, as in the present invention, this shift will occur down the length of the stent. This is a cumulative effect as one considers rotation of one end with respect to the other upon deployment. A stent delivery system, such as the one described below, will deploy the distal end first, then allow the proximal end to expand. It would be undesirable to allow the distal end to anchor into the vessel wall while holding the stent fixed in rotation, then release the proximal end. This could cause the stent to twist or whip in rotation to equilibrium after it is at least partially deployed within the vessel. Such whipping action may cause damage to the vessel.

However, one exemplary embodiment of the present invention, as illustrated in FIGS. **10** and **11**, reduces the chance of such events happening when deploying the stent. By mirroring the bridge geometry longitudinally down the stent, the rotational shift of the Z-sections or S-sections may be made to alternate and will minimize large rotational changes between any two points on a given stent during deployment or constraint. That is, the bridges **216** connecting loop **208**(*b*) to loop **208**(*c*) are angled upwardly from left to right, while the bridges connecting loop **208**(*c*) to loop **208**(*d*) are angled downwardly from left to right. This alternating pattern is

repeated down the length of the stent **200**. This alternating pattern of bridge slopes improves the torsional characteristics of the stent so as to minimize any twisting or rotation of the stent with respect to any two hoops. This alternating bridge slope is particularly beneficial if the stent starts to twist in vivo. As the stent twists, the diameter of the stent will change. Alternating bridge slopes tend to minimize this effect. The diameter of a stent having bridges which are all sloped in the same direction will tend to grow if twisted in one direction and shrink if twisted in the other direction. With alternating bridge slopes this effect is minimized and localized.

The feature is particularly advantageous for stents having large expansion ratios, which in turn requires them to have extreme bending requirements where large elastic strains are required. Nitinol, as stated above, can withstand extremely large amounts of elastic strain deformation, so the above features are well suited to stents made from this alloy. This feature allows for maximum utilization of Ni—Ti or other material properties to enhance radial strength, to improve stent strength uniformity, to improve fatigue life by minimizing local strain levels, to allow for smaller open areas which enhance entrapment of embolic material, and to improve stent apposition in irregular vessel wall shapes and curves.

Preferably, stents are laser cut from small diameter tubing. For prior art stents, this manufacturing process led to designs with geometric features, such as struts, loops and bridges, having axial widths W2, W1 and W3, respectively, which are larger than the tube wall thickness T (illustrated in FIG. **12**). When the stent is compressed, most of the bending occurs in the plane that is created if one were to cut longitudinally down the stent and flatten it out. However, for the individual bridges, loops and struts, which have widths greater than their thickness, there is a greater resistance to this in-plane bending than to out-of-plane bending. Because of this, the bridges and struts tend to twist, so that the stent as a whole may bend more easily. This twisting is a buckling condition which is unpredictable and can cause potentially high strain.

However, this problem has been solved in an exemplary embodiment of the present invention, as illustrated in FIGS. **10-14**. As seen from these figures, the widths of the struts, hoops and bridges are equal to or less than the wall thickness of the tube. Therefore, substantially all bending and, therefore, all strains are "out-of-plane." This minimizes twisting of the stent which minimizes or eliminates buckling and unpredictable strain conditions. This feature is particularly advantageous for stents having large expansion ratios, which in turn requires them to have extreme bending requirements where large elastic strains are required. Nitinol, as stated above, can withstand extremely large amounts of elastic strain deformation, so the above features are well suited to stents made from this alloy. This feature allows for maximum utilization of Ni—Ti or other material properties to enhance radial strength, to improve stent strength uniformity, to improve fatigue life by minimizing local strain levels, to allow for smaller open areas which enhance entrapment of embolic material, and to improve stent apposition in irregular vessel wall shapes and curves.

An alternate exemplary embodiment of a stent that may be utilized in conjunction with the present invention is illustrated in FIG. **15**. FIG. **15** shows stent **300** which is similar to stent **200** illustrated in FIGS. **10-14**. Stent **300** is made from a plurality of adjacent hoops **302**, FIG. **15** showing hoops **302** (*a*)-**302**(*d*). The hoops **302** include a plurality of longitudinal struts **304** and a plurality of loops **306** connecting adjacent struts, wherein adjacent struts are connected at opposite ends so as to form a substantially S or Z shape pattern. Stent **300** further includes a plurality of bridges **308** which connect adjacent hoops **302**. As seen from the figure, bridges **308** are non-linear and curve between adjacent hoops. Having curved bridges allows the bridges to curve around the loops and struts so that the hoops can be placed closer together which in turn, minimizes the maximum open area of the stent and increases its radial strength as well. This can best be explained by referring to FIG. **13**. The above described stent geometry attempts to minimize the largest circle which could be inscribed between the bridges, loops and struts, when the stent is expanded. Minimizing the size of this theoretical circle, greatly improves the stent because it is then better suited to trap embolic material once it is inserted into the patient.

As mentioned above, it is preferred that the stent of the present invention be made from a superelastic alloy and most preferably made of an alloy material having greater than 50.5 atomic percentage Nickel and the balance Titanium. Greater than 50.5 atomic percentage Nickel allows for an alloy in which the temperature at which the martensite phase transforms completely to the austenite phase (the Af temperature) is below human body temperature, and preferably is about twenty-four degrees C. to about thirty-seven degrees C., so that austenite is the only stable phase at body temperature.

In manufacturing the Nitinol stent, the material is first in the form of a tube. Nitinol tubing is commercially available from a number of suppliers including Nitinol Devices and Components, Fremont Calif. The tubular member is then loaded into a machine which will cut the predetermined pattern of the stent into the tube, as discussed above and as shown in the figures. Machines for cutting patterns in tubular devices to make stents or the like are well known to those of ordinary skill in the art and are commercially available. Such machines typically hold the metal tube between the open ends while a cutting laser, preferably under microprocessor control, cuts the pattern. The pattern dimensions and styles, laser positioning requirements, and other information are programmed into a microprocessor which controls all aspects of the process. After the stent pattern is cut, the stent is treated and polished using any number of methods or combination of methods well known to those skilled in the art. Lastly, the stent is then cooled until it is completely martensitic, crimped down to its un-expanded diameter and then loaded into the sheath of the delivery apparatus.

As stated in previous sections of this application, markers having a radiopacity greater than that of the superelastic alloys may be utilized to facilitate more precise placement of the stent within the vasculature. In addition, markers may be utilized to determine when and if a stent is fully deployed. For example, by determining the spacing between the markers, one can determine if the deployed stent has achieved its maximum diameter and adjusted accordingly utilizing a tacking process. FIG. **16** illustrates an exemplary embodiment of the stent **200** illustrated in FIGS. **10-14** having at least one marker on each end thereof. In a preferred embodiment, a stent having thirty-six struts per hoop can accommodate six markers **800**. Each marker **800** comprises a marker housing **802** and a marker insert **804**. The marker insert **804** may be formed from any suitable biocompatible material having a high radiopacity under X-ray fluoroscopy. In other words, the marker inserts **804** should preferably have a radiopacity higher than that of the material comprising the stent **200**. The addition of the marker housings **802** to the stent necessitates that the lengths of the struts in the last two hoops at each end of the stent **200** be longer than the strut lengths in the body of the stent to increase the fatigue life at the stent ends. The marker housings **802** are preferably cut from the same tube as the stent as briefly described above. Accordingly, the hous-

ings 802 are integral to the stent 200. Having the housings 802 integral to the stent 200 serves to ensure that the markers 800 do not interfere with the operation of the stent

FIG. 17 is a cross-sectional view of a marker housing 802. The housing 802 may be elliptical when observed from the outer surface as illustrated in FIG. 16. As a result of the laser cutting process, the hole 806 in the marker housing 802 is conical in the radial direction with the outer surface 808 having a diameter larger than the diameter of the inner surface 810, as illustrated in FIG. 17. The conical tapering in the marker housing 802 is beneficial in providing an interference fit between the marker insert 804 and the marker housing 802 to prevent the marker insert 804 from being dislodged once the stent 200 is deployed. A detailed description of the process of locking the marker insert 804 into the marker housing 802 is given below.

As set forth above, the marker inserts 804 may be made from any suitable material having a radiopacity higher than the superelastic material forming the stent or other medical device. For example, the marker insert 804 may be formed from niobium, tungsten, gold, platinum or tantalum. In the preferred embodiment, tantalum is utilized because of its closeness to nickel-titanium in the galvanic series and thus would minimize galvanic corrosion. In addition, the surface area ratio of the tantalum marker inserts 804 to the nickel-titanium is optimized to provide the largest possible tantalum marker insert, easy to see, while minimizing the galvanic corrosion potential. For example, it has been determined that up to nine marker inserts 804 having a diameter of 0.010 inches could be placed at the end of the stent 200; however, these marker inserts 804 would be less visible under X-ray fluoroscopy. On the other hand, three to four marker inserts 804 having a diameter of 0.025 inches could be accommodated on the stent 200; however, galvanic corrosion resistance would be compromised. Accordingly, in the preferred embodiment, six tantalum markers having a diameter of 0.020 inches are utilized on each end of the stent 200 for a total of twelve markers 800.

The tantalum markers 804 may be manufactured and loaded into the housing utilizing a variety of known techniques. In the exemplary embodiment, the tantalum markers 804 are punched out from an annealed ribbon stock and are shaped to have the same curvature as the radius of the marker housing 802 as illustrated in FIG. 17. Once the tantalum marker insert 804 is loaded into the marker housing 802, a coining process is used to properly seat the marker insert 804 below the surface of the housing 802. The coining punch is also shaped to maintain the same radius of curvature as the marker housing 802. As illustrated in FIG. 17, the coining process deforms the marker housing 802 material to lock in the marker insert 804.

As stated above, the hole 806 in the marker housing 802 is conical in the radial direction with the outer surface 808 having a diameter larger than the diameter of the inner surface 810 as illustrated in FIG. 17. The inside and outside diameters vary depending on the radius of the tube from which the stent is cut. The marker inserts 804, as stated above, are formed by punching a tantalum disk from annealed ribbon stock and shaping it to have the same radius of curvature as the marker housing 802. It is important to note that the marker inserts 804, prior to positioning in the marker housing 804, have straight edges. In other words, they are not angled to match the hole 806. The diameter of the marker insert 804 is between the inside and outside diameter of the marker housing 802. Once the marker insert 804 is loaded into the marker housing, a coining process is used to properly seat the marker insert 804 below the surface of the housing 802. In the preferred embodiment, the thickness of the marker insert 804 is less than or equal to the thickness of the tubing and thus the thickness or height of the hole 806. Accordingly, by applying the proper pressure during the coining process and using a coining tool that is larger than the marker insert 804, the marker insert 804 may be seated in the marker housing 802 in such a way that it is locked into position by a radially oriented protrusion 812. Essentially, the applied pressure, and size and shape of the housing tool forces the marker insert 804 to form the protrusion 812 in the marker housing 802. The coining tool is also shaped to maintain the same radius of curvature as the marker housing. As illustrated in FIG. 17, the protrusion 812 prevents the marker insert 804 from becoming dislodged from the marker housing.

It is important to note that the marker inserts 804 are positioned in and locked into the marker housing 802 when the stent 200 is in its unexpanded state. This is due to the fact that it is desirable that the tube's natural curvature be utilized. If the stent were in its expanded state, the coining process would change the curvature due to the pressure or force exerted by the coining tool.

As illustrated in FIG. 18, the marker inserts 804 form a substantially solid line that clearly defines the ends of the stent in the stent delivery system when seen under fluoroscopic equipment. As the stent 200 is deployed from the stent delivery system, the markers 800 move away from each other and flower open as the stent 200 expands as illustrated in FIG. 16. The change in the marker grouping provides the physician or other health care provider with the ability to determine when the stent 200 has been fully deployed from the stent delivery system.

It is important to note that the markers 800 may be positioned at other locations on the stent 200.

It is believed that many of the advantages of the present invention can be better understood through a brief description of a delivery apparatus for the stent, as shown in FIGS. 19 and 20. FIGS. 19 and 20 show a self-expanding stent delivery apparatus 10 for a stent made in accordance with the present invention. Apparatus 10 comprises inner and outer coaxial tubes. The inner tube is called the shaft 12 and the outer tube is called the sheath 14. Shaft 12 has proximal and distal ends. The proximal end of the shaft 12 terminates at a luer lock hub 16. Preferably, shaft 12 has a proximal portion 18 which is made from a relatively stiff material such as stainless steel, Nitinol, or any other suitable material, and a distal portion 20 which may be made from a polyethylene, polyimide, Pellethane, Pebax, Vestamid, Cristamid, Grillamid or any other suitable material known to those of ordinary skill in the art. The two portions are joined together by any number of means known to those of ordinary skill in the art. The stainless steel proximal end gives the shaft the necessary rigidity or stiffness it needs to effectively push out the stent, while the polymeric distal portion provides the necessary flexibility to navigate tortuous vessels.

The distal portion 20 of the shaft 12 has a distal tip 22 attached thereto. The distal tip 22 has a proximal end 24 whose diameter is substantially the same as the outer diameter of the sheath 14. The distal tip 22 tapers to a smaller diameter from its proximal end to its distal end, wherein the distal end 26 of the distal tip 22 has a diameter smaller than the inner diameter of the sheath 14. Also attached to the distal portion 20 of shaft 12 is a stop 28 which is proximal to the distal tip 22. Stop 28 may be made from any number of materials known in the art, including stainless steel, and is even more preferably made from a highly radiopaque material such as platinum, gold or tantalum. The diameter of stop 28 is substantially the same as the inner diameter of sheath 14,

and would actually make frictional contact with the inner surface of the sheath. Stop 28 helps to push the stent out of the sheath during deployment, and helps keep the stent from migrating proximally into the sheath 14.

A stent bed 30 is defined as being that portion of the shaft between the distal tip 22 and the stop 28. The stent bed 30 and the stent 200 are coaxial so that the distal portion 20 of shaft 12 comprising the stent bed 30 is located within the lumen of the stent 200. However, the stent bed 30 does not make any contact with stent 200 itself. Lastly, shaft 12 has a guidewire lumen 32 extending along its length from its proximal end and exiting through its distal tip 22. This allows the shaft 12 to receive a guidewire much in the same way that an ordinary balloon angioplasty catheter receives a guidewire. Such guidewires are well known in art and help guide catheters and other medical devices through the vasculature of the body.

Sheath 14 is preferably a polymeric catheter and has a proximal end terminating at a sheath hub 40. Sheath 14 also has a distal end which terminates at the proximal end 24 of distal tip 22 of the shaft 12, when the stent is in its fully un-deployed position as shown in the figures. The distal end of sheath 14 includes a radiopaque marker band 34 disposed along its outer surface. As will be explained below, the stent is fully deployed from the delivery apparatus when the marker band 34 is lined up with radiopaque stop 28, thus indicating to the physician that it is now safe to remove the apparatus 10 from the body. Sheath 14 preferably comprises an outer polymeric layer and an inner polymeric layer. Positioned between outer and inner layers is a braided reinforcing layer. Braided reinforcing layer is preferably made from stainless steel. The use of braided reinforcing layers in other types of medical devices can be found in U.S. Pat. No. 3,585,707 issued to Stevens on Jun. 22, 1971, U.S. Pat. No. 5,045,072 issued to Castillo et al. on Sep. 3, 1991, and U.S. Pat. No. 5,254,107 issued to Soltesz on Oct. 19, 1993.

FIGS. 19 and 20 illustrate the stent 200 as being in its fully un-deployed position. This is the position the stent is in when the apparatus 10 is inserted into the vasculature and its distal end is navigated to a target site. Stent 200 is disposed around stent bed 30 and at the distal end of sheath 14. The distal tip 22 of the shaft 12 is distal to the distal end of the sheath 14, and the proximal end of the shaft 12 is proximal to the proximal end of the sheath 14. The stent 200 is in a compressed state and makes frictional contact with the inner surface 36 of the sheath 14.

When being inserted into a patient, sheath 14 and shaft 12 are locked together at their proximal ends by a Tuohy Borst valve 38. This prevents any sliding movement between the shaft and sheath which could result in a premature deployment or partial deployment of the stent 200. When the stent 200 reaches its target site and is ready for deployment, the Tuohy Borst valve 38 is opened so that that the sheath 14 and shaft 12 are no longer locked together.

The method under which the apparatus 10 deploys the stent 200 is readily apparent. The apparatus 10 is first inserted into the vessel until the radiopaque stent markers 800 (front 202 and back 204 ends, see FIG. 16) are proximal and distal to the target lesion. Once this has occurred the physician would open the Tuohy Borst valve 38. The physician would then grasp hub 16 of shaft 12 so as to hold it in place. Thereafter, the physician would grasp the proximal end of the sheath 14 and slide it proximal, relative to the shaft 12. Stop 28 prevents the stent 200 from sliding back with the sheath 14, so that as the sheath 14 is moved back, the stent 200 is pushed out of the distal end of the sheath 14. As stent 200 is being deployed the radiopaque stent markers 800 move apart once they come out of the distal end of sheath 14. Stent deployment is complete when the marker 34 on the outer sheath 14 passes the stop 28 on the inner shaft 12. The apparatus 10 can now be withdrawn through the stent 200 and removed from the patient.

FIG. 21 illustrates the stent 200 in a partially deployed state. As illustrated, as the stent 200 expands from the delivery device 10, the markers 800 move apart from one another and expand in a flower like manner.

It is important to note that any of the above-described medical devices may be coated with coatings that comprise drugs, agents or compounds or simply with coatings that contain no drugs, agents or compounds. In addition, the entire medical device may be coated or only a portion of the device may be coated. The coating may be uniform or non-uniform. The coating may be discontinuous. However, the markers on the stent are preferably coated in a manner so as to prevent coating buildup which may interfere with the operation of the device.

In a preferred exemplary embodiment, the self-expanding stents, described above, may be coated with a rapamycin containing polymer. In this embodiment, the polymeric coated stent comprises rapamycin in an amount ranging from about fifty to one-thousand micrograms per square centimeter surface area of the vessel that is spanned by the stent. The rapamycin is mixed with the polyvinylidenefluoride-hexafluoropropylene polymer (described above) in the ratio of drug to polymer of about thirty/seventy. The polymer is made by a batch process using the two monomers, vinylidene fluoride and hexafluoropropylene under high pressure by an emulsion polymerization process. In an alternate exemplary embodiment, the polymer may be made utilizing a batch dispersion process. The polymeric coating weight itself is in the range from about two-hundred to about one thousand seven hundred micrograms per square centimeter surface area of the vessel that is spanned by the stent.

The coated stent comprises a base coat, commonly referred to as a primer layer. The primer layer typically improves the adhesion of the coating layer that comprises the rapamycin. The primer also facilitates uniform wetting of the surface thereby enabling the production of a uniform rapamycin containing coating. The primer layer may be applied using any of the above-described techniques. It is preferably applied utilizing a dip coating process. The primer coating is in the range from about one to about ten percent of the total weight of the coating. The next layer applied is the rapamycin containing layer. The rapamycin containing layer is applied by a spin coating process and subsequently dried in a vacuum oven for approximately sixteen hours at a temperature in the range from about fifty to sixty degrees centigrade. After drying or curing, the stent is mounted onto a stent delivery catheter using a process similar to the uncoated stent. The mounted stent is then packaged and sterilized in any number of ways. In one exemplary embodiment, the stent is sterilized using ethylene oxide.

As described above, various drugs, agents or compounds may be locally delivered via medical devices. For example, rapamycin and heparin may be delivered by a stent to reduce restenosis, inflammation, and coagulation. Various techniques for immobilizing the drugs, agents or compounds are discussed above, however, maintaining the drugs, agents or compounds on the medical devices during delivery and positioning is critical to the success of the procedure or treatment. For example, removal of the drug, agent or compound coating during delivery of the stent can potentially cause failure of the device. For a self-expanding stent, the retraction of the restraining sheath may cause the drugs, agents or compounds to rub off the stent. For a balloon expandable stent, the expansion of the balloon may cause the drugs, agents or compounds

to simply delaminate from the stent through contact with the balloon or via expansion. Therefore, prevention of this potential problem is important to have a successful therapeutic medical device, such as a stent.

There are a number of approaches that may be utilized to substantially reduce the above-described concern. In one exemplary embodiment, a lubricant or mold release agent may be utilized. The lubricant or mold release agent may comprise any suitable biocompatible lubricious coating. An exemplary lubricious coating may comprise silicone. In this exemplary embodiment, a solution of the silicone base coating may be introduced onto the balloon surface, onto the polymeric matrix, and/or onto the inner surface of the sheath of a self-expanding stent delivery apparatus and allowed to air cure. Alternately, the silicone based coating may be incorporated into the polymeric matrix. It is important to note, however, that any number of lubricious materials may be utilized, with the basic requirements being that the material be biocompatible, that the material not interfere with the actions/effectiveness of the drugs, agents or compounds and that the material not interfere with the materials utilized to immobilize the drugs, agents or compounds on the medical device. It is also important to note that one or more, or all of the above-described approaches may be utilized in combination.

Referring now to FIG. **22**, there is illustrated a balloon **400** of a balloon catheter that may be utilized to expand a stent in situ. As illustrated, the balloon **400** comprises a lubricious coating **402**. The lubricious coating **402** functions to minimize or substantially eliminate the adhesion between the balloon **400** and the coating on the medical device. In the exemplary embodiment described above, the lubricious coating **402** would minimize or substantially eliminate the adhesion between the balloon **400** and the heparin or rapamycin coating. The lubricious coating **402** may be attached to and maintained on the balloon **400** in any number of ways including but not limited to dipping, spraying, brushing or spin coating of the coating material from a solution or suspension followed by curing or solvent removal step as needed.

Materials such as synthetic waxes, e.g. diethyleneglycol monostearate, hydrogenated castor oil, oleic acid, stearic acid, zinc stearate, calcium stearate, ethylenebis (stearamide), natural products such as paraffin wax, spermaceti wax, carnuba wax, sodium alginate, ascorbic acid and flour, fluorinated compounds such as perfluoroalkanes, perfluorofatty acids and alcohol, synthetic polymers such as silicones e.g. polydimethylsiloxane, polytetrafluoroethylene, polyfluoroethers, polyalkylglycol e.g. polyethylene glycol waxes, and inorganic materials such as talc, kaolin, mica, and silica may be used to prepare these coatings. Vapor deposition polymerization e.g. parylene-C deposition, or RF-plasma polymerization of perfluoroalkenes and perfluoroalkanes can also be used to prepare these lubricious coatings.

FIG. **23** illustrates a cross-section of a band **102** of the stent **100** illustrated in FIG. **1**. In this exemplary embodiment, the lubricious coating **500** is immobilized onto the outer surface of the polymeric coating. As described above, the drugs, agents or compounds may be incorporated into a polymeric matrix. The stent band **102** illustrated in FIG. **23** comprises a base coat **502** comprising a polymer and rapamycin and a top coat **504** or diffusion layer **504** also comprising a polymer. The lubricious coating **500** is affixed to the top coat **502** by any suitable means, including but not limited to spraying, brushing, dipping or spin coating of the coating material from a solution or suspension with or without the polymers used to create the top coat, followed by curing or solvent removal step as needed. Vapor deposition polymerization and RF-plasma polymerization may also be used to affix those lubricious coating materials that lend themselves to this deposition method, to the top coating. In an alternate exemplary embodiment, the lubricious coating may be directly incorporated into the polymeric matrix.

If a self-expanding stent is utilized, the lubricious coating may be affixed to the inner surface of the restraining sheath. FIG. **24** illustrates a self-expanding stent **200** (FIG. **10**) within the lumen of a delivery apparatus sheath **14**. As illustrated, a lubricious coating **600** is affixed to the inner surfaces of the sheath **14**. Accordingly, upon deployment of the stent **200**, the lubricious coating **600** preferably minimizes or substantially eliminates the adhesion between the sheath **14** and the drug, agent or compound coated stent **200**.

In an alternate approach, physical and/or chemical cross-linking methods may be applied to improve the bond strength between the polymeric coating containing the drugs, agents or compounds and the surface of the medical device or between the polymeric coating containing the drugs, agents or compounds and a primer. Alternately, other primers applied by either traditional coating methods such as dip, spray or spin coating, or by RF-plasma polymerization may also be used to improve bond strength. For example, as shown in FIG. **25**, the bond strength can be improved by first depositing a primer layer **700** such as vapor polymerized parylene-C on the device surface, and then placing a second layer **702** which comprises a polymer that is similar in chemical composition to the one or more of the polymers that make up the drug-containing matrix **704**, e.g., polyethylene-co-vinyl acetate or polybutyl methacrylate but has been modified to contain cross-linking moieties. This secondary layer **702** is then cross-linked to the primer after exposure to ultra-violet light. It should be noted that anyone familiar with the art would recognize that a similar outcome could be achieved using cross-linking agents that are activated by heat with or without the presence of an activating agent. The drug-containing matrix **704** is then layered onto the secondary layer **702** using a solvent that swells, in part or wholly, the secondary layer **702**. This promotes the entrainment of polymer chains from the matrix into the secondary layer **702** and conversely from the secondary layer **702** into the drug-containing matrix **704**. Upon removal of the solvent from the coated layers, an interpenetrating or interlocking network of the polymer chains is formed between the layers thereby increasing the adhesion strength between them. A top coat **706** is used as described above.

A related difficulty occurs in medical devices such as stents. In the drug-coated stents crimped state, some struts come into contact with each other and when the stent is expanded, the motion causes the polymeric coating comprising the drugs, agents or compounds to stick and stretch. This action may potentially cause the coating to separate from the stent in certain areas. The predominant mechanism of the coating self-adhesion is believed to be due to mechanical forces. When the polymer comes in contact with itself, its chains can tangle causing the mechanical bond, similar to hook and loop fasteners such as Velcro®. Certain polymers do not bond with each other, for example, fluoropolymers. For other polymers, however, powders may be utilized. In other words, a powder may be applied to the one or more polymers incorporating the drugs, agents or other compounds on the surfaces of the medical device to reduce the mechanical bond. Any suitable biocompatible material which does not interfere with the drugs, agents, compounds or materials utilized to immobilize the drugs, agents or compounds onto the medical device may be utilized. For example, a dusting with a water soluble powder may reduce the tackiness of the coatings surface and this will prevent the polymer from sticking to

itself thereby reducing the potential for delamination. The powder should be water-soluble so that it does not present an emboli risk. The powder may comprise an anti-oxidant, such as vitamin C, or it may comprise an anti-coagulant, such as aspirin or heparin. An advantage of utilizing an anti-oxidant may be in the fact that the anti-oxidant may preserve the other drugs, agents or compounds over longer periods of time.

It is important to note that crystalline polymers are generally not sticky or tacky. Accordingly, if crystalline polymers are utilized rather than amorphous polymers, then additional materials may not be necessary. It is also important to note that polymeric coatings without drugs, agents, and/or compounds may improve the operating characteristics of the medical device. For example, the mechanical properties of the medical device may be improved by a polymeric coating, with or without drugs, agents and/or compounds. A coated stent may have improved flexibility and increased durability. In addition, the polymeric coating may substantially reduce or eliminate galvanic corrosion between the different metals comprising the medical device.

Any of the above-described medical devices may be utilized for the local delivery of drugs, agents and/or compounds to other areas, not immediately around the device itself. In order to avoid the potential complications associated with systemic drug delivery, the medical devices of the present invention may be utilized to deliver therapeutic agents to areas adjacent to the medical device. For example, a rapamycin coated stent may deliver the rapamycin to the tissues surrounding the stent as well as areas upstream of the stent and downstream of the stent. The degree of tissue penetration depends on a number of factors, including the drug, agent or compound, the concentrations of the drug and the release rate of the agent.

The drug, agent and/or compound/carrier or vehicle compositions described above may be formulated in a number of ways. For example, they may be formulated utilizing additional components or constituents, including a variety of excipient agents and/or formulary components to affect manufacturability, coating integrity, sterilizability, drug stability, and drug release rate. Within exemplary embodiments of the present invention, excipient agents and/or formulary components may be added to achieve both fast-release and sustained-release drug elution profiles. Such excipient agents may include salts and/or inorganic compounds such as acids/bases or buffer components, anti-oxidants, surfactants, polypeptides, proteins, carbohydrates including sucrose, glucose or dextrose, chelating agents such as EDTA, glutathione or other excipients or agents.

Although shown and described is what is believed to be the most practical and preferred embodiments, it is apparent that departures from specific designs and methods described and shown will suggest themselves to those skilled in the art and may be used without departing from the spirit and scope of the invention. The present invention is not restricted to the particular constructions described and illustrated, but should be constructed to cohere with all modifications that may fall within the scope of the appended claims.

What is claimed is:

1. A device for intraluminal implantation in a vessel comprising a balloon-expandable stent and a pharmaceutical agent-containing coating, said coating comprising a biocompatible polyfluoro copolymer that comprises about eighty-five weight percent vinylidinefluoride copolymerized with about fifteen weight percent hexafluoropropylene and at least one pharmaceutical agent intermixed with said copolymer, wherein said coating has not been subjected to a maximum temperature greater than 60° C. during the coating process or afterward, thereby providing an adherent coating that remains adhered to the device upon expansion of the balloon-expandable stent.

2. A device according to claim 1 wherein said polyfluoro copolymer consists of 85.5 weight percent vinylidinefluoride copolymerized with 14.5 weight percent hexafluoropropylene.

3. A device according to claim 1 wherein said pharmaceutical agent and said copolymer are selected to release said pharmaceutical agent for at least 800 hours following intraluminal implantation.

4. A device according to claim 3 wherein said agent is present in an amount that is from about 12% to about 20% by weight of the coating.

5. A device according to claim 1 wherein said pharmaceutical agent and said copolymer are selected to release said agent for at least 2000 hours following intraluminal implantation.

6. A device according to claim 5 wherein said agent is present in an amount that is from about 12% to about 20% by weight of the coating.

7. A device according to claim 1 wherein said pharmaceutical agent is present in an amount that is from about 12% to about 20% by weight of the coating.

8. A device according to claim 7 wherein said polyfluoro copolymer consists of 85.5 weight percent vinylidinefluoride copolymerized with 14.5 weight percent hexafluoropropylene.

9. A device according to claim 7 that releases said agent at a rate of about 0.001 $\mu g/cm^2$-min to about 100 $\mu g/cm^2$-min.

10. A device according to claim 1 that releases said pharmaceutical agent at a rate of about 0.001 $\mu g/cm^2$-min to about 100 $\mu g/cm^2$-min.

11. A device according to claim 1 wherein said at least one pharmaceutical agent is present in an amount effective to reduce restenosis.

12. A device according to claim 11 wherein said device releases said agent for at least 800 hours following intraluminal implantation.

13. A device according to claim 12 wherein said agent is present in an amount that is from about 12% to about 20% by weight of the coating.

14. A device according to claim 12 wherein said coating releases said agent at a rate of about 0.001 $\mu g/cm^2$-min to about 100 $\mu g/cm^2$-min.

15. The device according to any one of claims 1 to 8, 10, 9 or 11 to 14, wherein said pharmaceutical agent is an immunosuppressive.

16. The device according to any one of claims 1 to 8, 10, 9 or 11 to 14, wherein said pharmaceutical agent is an mTOR inhibitor.

17. The device according to any one of claims 1 to 8, 10, 9 or 11 to 14, wherein said pharmaceutical agent is rapamycin.

18. The device according to any one of claims 1 to 8, 10, 9 or 11 to 14, wherein said pharmaceutical agent is a macrocyclic triene analog of rapamycin that binds FKBP12.

19. A method for preparing a device for providing prolonged release of a pharmaceutical agent when implanted in a vessel, said method comprising the steps of:

combining said pharmaceutical agent with a biocompatible polyfluoro copolymer that comprises about eighty-five weight percent vinylidinefluoride copolymerized with about fifteen weight percent hexafluoropropylene to provide a coating;

applying said coating to a balloon-expandable stent; and

drying the balloon-expandable stent comprising said coating at a maximum temperature no greater than 60° C. to

thereby provide an adherent coating that remains adhered to the device upon expansion of the balloon-expandable stent.

20. A method according to claim 19, wherein said polyfluoro copolymer consists of 85.5 weight percent vinylidine-fluoride copolymerized with 14.5 weight percent hexafluoropropylene.

21. The method according to claim 20, wherein said pharmaceutical agent is an immunosuppressive.

22. The method according to claim 20, wherein said pharmaceutical agent is an mTOR inhibitor.

23. The method according to claim 20, wherein said pharmaceutical agent is rapamycin.

24. The method according to claim 20, wherein said pharmaceutical agent is a macrocyclic triene analog of rapamycin that binds FKBP12.

* * * * *

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional)

In re Application of: Gerard H. Llanos, et al.

Application No.: 11/941,351

Filed: 11/16/07

For: MEDICAL DEVICES, DRUG COATINGS AND METHODS FOR MAINTAINING THE DRUG COATINGS THEREON

The owner*, CORDIS CORPORATION, of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term **prior patent** No. 7,056,550 as the term of said prior patent is defined in 35 U.S.C. 154 and 173, and as the term of said **prior patent** is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

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expires for failure to pay a maintenance fee;
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/S. Maurice Valla/ — August 7, 2008
Signature — Date

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CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION

I certify that I am counsel for Appellant Cordis Corporation and that the foregoing OPENING BRIEF OF APPELLANT CORDIS CORPORATION complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B). The OPENING BRIEF contains 13,613 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii).

Dated: August 17, 2015

/s/ Joseph Lucci
Joseph Lucci
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CERTIFICATE OF SERVICE

I hereby certify that I filed the foregoing OPENING BRIEF OF APPELLANT CORDIS CORPORATION with the U.S. Court of Appeals for the Federal Circuit via CM/ECF and served a copy on counsel of record via email to:

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